



*Project Synopses*



**KA1**

**Food,  
Nutrition  
& Health**

**Volume 2**



QUALITY OF LIFE AND MANAGEMENT  
OF LIVING RESOURCES

**FIFTH FRAMEWORK  
PROGRAMME  
1998-2002**

**QUALITY OF LIFE AND  
MANAGEMENT OF LIVING RESOURCES**



**PROJECT SYNOPSES**

October 2002

**Key Action 1  
Food, Nutrition and Health**

**Volume 1 comprises Areas 1 and 2  
Volume 2 comprises Area 3**

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## FOREWORD

The food and drink sector is a leading sector in the EU in terms of industrial value and output. It employs 2,6 million people<sup>1</sup>, and its turnover is worth € 700 billion<sup>2</sup>. The overall objectives of Key Action 1 “Food, nutrition and health” within the Programme “Quality of Life and Management of Living Resources” are to strengthen research in the agriculture, fisheries and food sector in universities, research centres and the industry. This will ensure that Europe maintains its strong position in this field into the future. By its funding of European projects and its links to national research activities on these topics, this key action aims to lead to a better understanding of consumers’ needs to provide a healthy, safe and high quality food supply leading to reinforced consumer confidence in the safety and wholesomeness of the European food supply.

The Key Action “Food, Nutrition and Health” with an overall budget of € 290 million has built upon earlier EU funding of research in food science in the FLAIR, AIR and FAIR RTD programmes of the European Commission. However, the research priorities and objectives have evolved considerably from previous programmes and in this key action the following three objectives were tackled:

- Addressing consumer needs and enhancing the competitiveness of the European food industry;
- Assuring the safety and integrity of the food supply;
- Understanding the role of nutrition in health and well being.

There has been an excellent response from researchers, industries and consumers to the research priorities defined, and now there is a comprehensive portfolio of collaborative projects funded and running. Cluster type projects were introduced in this key action, which are now running and producing valuable results. The External Advisory Group for Key Actions 1 and 4 and the Quality of Life Programme Committee has played an important role in the planning and implementation of this key action.

This catalogue gives details of all the running projects, but is also a useful guide to many of the principal research teams involved in food research in Europe. Most of the projects have a web site address, which can easily be accessed and gives further information on the project.

I hope the reader will find this publication both interesting and useful.

**Bruno Hansen**  
**Director “Biotechnology, Agriculture and Food”**  
**Brussels, October 2002**

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<sup>1</sup> Eurostat Yearbook 2001

<sup>2</sup> Panorama of European Business. Eurostat 2000.



## **PREFACE FROM EAG CHAIR**

It has been my pleasure over the last four years to chair the External Advisory Group (EAG) for the Key Actions “Food, Nutrition and Health” and “Environment and Health” of the Fifth Framework Programme (FP5), Quality of Life and Management of Living Resources. Our task has been to provide external independent advice to the Commission. Our advice has focused primarily on research priorities and annual revision of the Work Programme.

Our EAG was composed of 23 experts drawn from university medical and food faculties (e.g. occupational, environmental medicine departments), national institutes of public health, research institutes, health authorities, food industry, etc. The broad range of expertise and of geographical backgrounds guaranteed that we had appropriate experience available. Furthermore, we could call on networks of scientific peers to give guidelines for the detailed work programmes of FP5, to comment on the projects funded and to make the Commission aware of the latest scientific opportunities and high-priority areas for the European Union.

This advice has been provided on a continuous basis to the Commission services during the implementation of FP5 and has been particularly used in the annual revisions of the work programmes. The group has also focused on a number of emerging issues in the fields of both key actions and more detailed workshops in those areas were held. It has been particularly important to have these opportunities for focused workshops to ensure that funding is directed towards areas of major societal concern, including food and environmental safety, as well as identifying opportunities for future exploitation, such as nutritional genomics. We believe the work of the group has been useful and relevant and has helped considerably in the running and implementation of both key actions and is reflected in the projects funded and featured in this catalogue.

We also believe that information to, and involvement of, the public needs to be further improved. Therefore we have been helping and encouraging the European Commission and the research teams involved to make available the results and conclusions of the research to a wider public. This catalogue provides one such means of dissemination of information. Our hope is that through our contribution but primarily through the research supported, the results generated and their application, we might improve the quality of life of Europeans and other populations.

**Professor Christine Williams**  
**Chair of the External Advisory Group**  
**Quality of Life Programme, Key Actions 1 and 4**



## INTRODUCTION

Key Action 1 “Food, Nutrition and Health” aims to provide a better understanding of consumer requirements and a healthy, safe and high quality food supply while improving the competitiveness of the European food industry.

The key action is organised into three main areas, which in turn are organised in sub-areas:

Area 1: Development of safe and flexible and new and/or improved manufacturing processes and technologies

1.1 Novel and improved biological raw materials for high quality food;

1.2 Advanced and optimised food technologies, packaging systems and process control;

1.3 Quality monitoring and traceability throughout the food chain.

Area 2: Development of tests to detect and processes to eliminate infectious and toxic agents throughout the food chain

2.1. Improved understanding and control of contamination conditions arising along the entire food chain from primary producer to consumer;

2.2. Rapid detection tests particularly for pathogens and hormones;

2.3. New and safer methods of food production and distribution;

2.4. New methodologies for assessing microbial, chemical and allergenic risks and exposures.

Area 3: Research into the role of food in promoting and sustaining health with respect to diet and nutrition, toxicology, epidemiology, environmental interaction, consumer choice and public health

3.1. Consumer needs, attitudes and responses with regard to food products, food processing and labelling;

3.2. Role and impact of food on physiological functions, physical and mental performance;

3.3. Particular nutritional needs of defined population groups;

3.4. Links between diet and chronic diseases and disorders including the genetic factors involved.

Within the four calls of the Programme “Quality of Life and Management of Living Resources Programme” from 1999 to 2001, six deadlines for submission have been open for proposals for Key Action 1. This catalogue contains synopses of all of the projects that are funded following these deadlines. The projects have been sorted per area and listed by contract number within an area. Table 1 shows the number of projects submitted and selected by area for each deadline with the corresponding EU contribution.

The budget for Key Action 1 is € 290 million for the four-year period 1998 to 2002. The financial contribution from the EU for the 151 research and development projects selected amounts to € 239 million, which represents 82% of the total budget of the key action. The remainder of the budget goes to SME Specific Measures, Accompanying Measures, Training Grants, and administration.

**TABLE 1: NUMBER OF PROJECTS SUBMITTED AND SELECTED BY AREA**

Area	Deadline	Number of proposals received	Number of proposals selected	EC contribution (€ million)
Area 1: Technology and raw materials	November 1999	182	18	24,6
	October 2000	160	15	19,0
	January 2002	107	17	26,7
	Subtotal	449	50	70,5
Area 2: Food safety	June 1999	74	21	29,6
	November 1999	35	4	2,9
	October 2000	62	15	19,2
	January 2002	23	5	5,8
	Subtotal	194	45	57,7
Area 3: Role of food in promoting health	June 1999	115	18	36,9
	March 2000	123	18	32,0
	March 2001	99	15	28,2
	January 2002	37	7	13,4
	Subtotal	374	56	110,5
Total		1017	151	236,6

Different types of actions are supported by KA1: Shared-Cost Actions, Thematic Networks, Concerted Actions, Training Fellowships, and Accompanying Measures. This publication contains only the three first types of actions. They are subdivided as following in:

- 137 Shared-Cost Actions, which include Research & Development projects, Demonstrations Projects, Combined R&D and demonstrations projects, and support for access to research infrastructures. This represents a total EU contribution of € 218.0 million.
- 4 Thematic Networks representing a total EU contribution of € 4.1 million.
- 12 Concerted Actions representing a total EU contribution of € 16.7 million.

A number of research projects that are focussed on a common subject have formed large clusters.

The average number of participants per project is nine. About 27% of the participants are companies. In 70% of the projects, at least one industrial partner is involved.

The objective of this publication is not to assess the projects or the results generated, but to give an overview on the ongoing research being carried out in Key Action 1 “Food, Nutrition and Health”.

This catalogue has been edited and compiled by Rosanna D’Amario, Isabelle de Froidmont-Görtz, Barbara Rens and Jürgen Lucas with the help of all Scientific Officers mentioned below. The European Commission would like to thank the coordinators of the projects for the replies to the requests and for supplying so many interesting photographs to complement the text of this publication.

**Liam Breslin**  
**Head of Unit DG Research E.2 “Health, Food and Environment”**  
**Brussels, October 2002**

## **ABBREVIATIONS**

### **Country codes**

A	Austria
AUS	Australia
B	Belgium
BG	Bulgaria
CA	Canada
CH	Switzerland
CZ	Czech Republic
D	Germany
DK	Denmark
E	Spain
EE	Estonia
FIN	Finland
F	France
GB	United Kingdom
GR	Greece
HU	Hungary
IL	Israel
IRL	Ireland
IS	Iceland
I	Italy
LU	Luxembourg
LT	Lithuania
LV	Latvia
NL	The Netherlands
NO	Norway
PL	Poland
P	Portugal
RO	Romania
SI	Slovenia
SK	Slovakia
S	Sweden
USA	USA

### **Types of projects**

SC	Shared cost actions
CA	Concerted actions
CM	Combined projects
SD	Demonstration project
TN	Thematic network



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### **AREA 3.**

**Research into the role of food in promoting and sustaining health with respect to diet and nutrition, toxicology, epidemiology, environmental interaction, consumer choice and public health**

**Healthy ageing: How changes in sensory physiology, sensory psychology and socio-cognitive factors influence food choice**  
**HEALTHSENSE-CHOICE**

**Contract number:** QLK1-1999-00010

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## **Healthy ageing: How changes in sensory physiology, sensory psychology and socio-cognitive factors influence food choice**

### **BACKGROUND**

A major societal challenge is to improve the quality of life and reduce disability and dependency in the ageing population. Large variations in age-adjusted incidence of major chronic diseases suggest strong environmental determinants, including diet. However, the consumer is the final judge of the acceptability of a food. Therefore, healthy ageing among all groups, but particularly in older people, will not be possible until the physiological factors and mechanisms of food choice and acceptance have been studied. This cluster project will define the sensory psychobiology, cognitive and social determinants of food choice, intake and enjoyment in different age groups and cultures. The data obtained will help to develop future nutrition policy and will improve the competitiveness of the EU food and drink sector.

### **OBJECTIVES**

- To determine the degree and nature of changes, which occur during ageing, in the physiological capability of the senses which are used to perceive texture, other mouthfeel stimuli, odour and taste, and determine the influence of these changes in food perception
- To understand the functioning of sensory memory and its role in food perception
- To determine the influence of changes in sensory capability on food appreciation, and food intake in different situations
- To provide information on the impact of sensory physiological ageing on choice of food
- To understand the attitudes of elderly people with respect to issues relating to food choice, and how these may affect their behaviour
- To understand the provisioning of food with respect to elderly people, and how this impinges on food choice
- To determine the special needs of elderly people with respect to factors such as packaging, portion sizes, ease of preparation, pricing, social context, etc.
- To establish the relative importance of sensory quality as a choice criterion versus other criteria, such as price, healthiness, branding etc.
- To understand demographic and cross-cultural differences, both qualitatively and quantitatively, with respect to the issues raised above
- To determine the difference between needs of full and part-time resident elderly people in a Mediterranean country
- To identify improvements that can be made to food products to increase their acceptability
- To provide guidelines to inform policy makers, the food industry and consumer groups who support the elderly on ways to develop and promote new food products that are both attractive and nutritionally tailored to older people
- To contribute to the health and well-being of the rapidly growing population of ageing people in Europe.

## (EXPECTED) RESULTS AND ACHIEVEMENTS

The project will:

- meet the aspirations of the consumer by providing the scientific basis for foods which will promote well-being
- contribute knowledge, which will be essential in realising the potential socio-economic benefits of promoting health through food
- provide a basis for developing food and nutritional policies within the EU, also in relation to the ageing population
- provide knowledge of physiological constraints, knowledge of changes in sensory perception and the value of sensory product attributes which will contribute to the targeting of commercial and public efforts to promote improved dietary intakes, health status and quality of life among EU consumers

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QLK1-1999-00010: Healthy ageing: How changes in sensory physiology, sensory psychology and socio-cognitive factors influence food choice

**Evaluation of the prevalence of the coeliac disease and its genetic  
components in the European population  
COELIAC-EU/CLUSTER**

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## **Evaluation of the prevalence of the coeliac disease and its genetic components in the European population**

### **BACKGROUND**

Coeliac disease is an autoimmune disease triggered in genetically predisposed individuals by gluten adsorption (gluten is a ubiquitous component of cereals and as such is broadly found in many foods). In genetically susceptible individuals, gluten ingestion results in intestinal mucosa damage and malabsorption of essential nutrients. As of today, a life-long gluten-free diet is the only therapy available. Preliminary data obtained during the last few years have shown that the prevalence of coeliac disease is more frequent in the European population than originally estimated from the clinical symptomatology. The cluster project is devoted to better appreciate at the EU level the prevalence of the disease under its different symptomatic forms, to decipher the genetic components of the disease and to study the pathogenesis of the disease by testing the molecular hypothesis built on the most recent immunological discoveries.

### **OBJECTIVES**

The Coeliac-EU cluster groups together three research projects with complementary principal scientific objectives:

- 1) To establish the prevalence of coeliac disease in a large European population;
- 2) To characterise the genetic basis of this common food intolerance;
- 3) To identify factors involved in the gluten-triggered pathogenesis of mucosal damage.

### **(EXPECTED) RESULTS AND ACHIEVEMENTS**

The EPIDEMIOLOGY study will provide an estimate of the prevalence of coeliac disease in Europe and allow identification and early treatment of 'silent' coeliac people who are so far not detected. The detection relies on two anti-tissue transglutaminase test kits, one based on guinea-pig and one on human. The detection kits have been extensively studied and validated in ring tests. At this stage, the human based test looks slightly more specific than the guinea-pig-based test, with comparable sensitivity. The large-scale comparative evaluation will be started as soon as the gathering of the retrospective sera will be completed. 5.766 retrospective sera have already been sampled. 13.400 new sera have already been collected for the prevalence determination study, which has already started in advance of the timetable. Self-administered questionnaires for the antibody positive individuals will allow recording of the basic data of signs and symptoms of these individuals, which will be valuable information when describing the results of the study.

The GENETIC study will identify association(s) between gene(s) and the coeliac disease as well as clarify the contribution of the HLA genetic components and their association with other (non-HLA) genetic markers. DNA samples from 623 simplex families and 548 sib-pair families have been assembled. Two-third of the HLA typing was carried out. Fine HLA typing of the DQ2 negative group is proceeding in each of the five centres and is already finished in some of those.

The PATHOGENESIS study will characterise features of damage in the coeliac mucosa and provide information on factors involved in the pathogenesis of mucosal dam-

age, in particular on T cells involvement. The cytokine pattern in the organ culture system of the treated coeliac mucosa has been refined: the dominance of gamma interferon indicate a strongly Th1 polarised response to gluten. Molecules candidate to drive such a response are IL15, IL18 and possibly  $\epsilon$ -interferon. Induction of epithelial cells apoptosis as an early gluten triggered response has been demonstrated to involve FAS. This appears to be an essential factor in the pathogenic process leading to mucosal damage. Genes sequences up and down regulated by transforming growth factor-beta in the fibroblasts-epithelial cell co-culture model have been isolated and studied. Their relevance in the apoptotic process is suggestive but remain to be directly demonstrated.

A new simple serological diagnostic test, suitable for large population screening and allowing an easier and earlier detection of the disease, will be validated. A non-invasive genetic test based on DNA analysis may potentially be developed in the future. New therapeutic strategies, for instance based on immunomodulation, may potentially be developed in the future.

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PREVALENCE OF THE COELIAC DISEASE AND ITS GENETIC COMPONENTS IN THE EUROPEAN POPULATION

## COELIAC-EU CLUSTER

# No QLK1 - CT - 1999 - 00037



QLK1-1999-00037: Evaluation of the prevalence of the coeliac disease and its genetic components in the European population

**Conjugated linoleic acid (CLA) in functional food:  
A potential benefit for overweight middle-aged Europeans  
FUNCLA**

**Contract number:** QLK1-1999-00076  
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## **Conjugated linoleic acid (CLA) in functional food: A potential benefit for overweight middle-aged Europeans**

### **BACKGROUND**

Overweight in middle-aged populations is an increasing factor in EU health-care costs. Overweight causes a loss of self-esteem, is socially disadvantageous and increases the incidence of diabetes, dyslipidaemia and coronary heart disease. Conjugated linoleic acid (CLA) can reduce body fat. This project aims to formulate a functional food containing an active CLA-isomer that will reduce overweight and improve health. Human experiments will determine which CLA isomer is active and which form has highest bioavailability. Pure CLA isomers, stable isotope-labelled CLA and a functional food containing CLA will be fed to middle-aged people including overweight subjects with no disease and to patients with diabetes or hyperlipidaemia. Complementary studies will use an animal model.

### **OBJECTIVES**

The main objective of this project is to develop a functional food containing conjugated linoleic acid, designed to reduce overweight and the negative impact of overweight on the health of the middle-aged population. The scientific objectives of the project are: 1) to assess the impact of conjugated linoleic acid (CLA) isomers on the energy metabolism and fat partitioning in overweight humans; 2) to assess the bioavailability of CLA isomers in humans, including the absorption and the utilisation of CLA as energy fuel; 3) to determine which of the CLA isomer(s) is (are) active; 4) to assess the impact of the active CLA isomer(s) on different health parameters and to determine any possible side effects. The technological objectives are 1) to develop a functional food containing the active CLA isomer(s) and to assess the metabolic impact on humans; 2) to assess the acceptability of the functional food for the consumer, including sensory evaluation.

### **(EXPECTED) RESULTS AND ACHIEVEMENTS**

The bioavailability of a mixture of 2 CLA isomers present as free fatty acid, ethyl esters, and triacylglycerols was tested. The raw data indicate that the ethyl ester was less well incorporated than the other forms with little difference between the free fatty acid and the TAG. Due to palatability and possibly oxidation problems with the free fatty acid, TAG is the form to be used.

Large scale preparations of the pure CLA isomers as TAG were developed and used to produce the drinkable preparation necessary for the trials in 2001. Together with four external experts in toxicology it was decided to lower the CLA dosage and to reinforce the safety of the protocol of the human study after an external publication appeared at the end of 2000 showing potential side effects of CLA.

Two rat studies were carried out in order to determine whether exercise would enhance the effects of CLA and to obtain complementary knowledge on the effects of CLA on energy metabolism. The data suggest that CLA may induce stimulation of AT and muscle protein turnover, which increases energy expenditure and could be involved in AT mass reduction.

Oxidation of CLA isomers was determined using <sup>14</sup>C isomers of 9c,11t- and 10t,12c-CLA. The data indicated that both CLA isomers were oxidised significantly more than linoleic acid. Moreover, less radioactivity was recovered in most tissues after CLA intake than after linoleic acid intake.

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QLK1-1999-00076: Conjugated linoleic acid (CLA) in functional food: A potential benefit for overweight middle-aged Europeans

**Functional properties, bioactivities and bioavailability of  
phytochemicals, especially anthocyanins, from processed foods  
ANTHOCYANIN BIOACTIVITIES**

**Contract number:** QLK1-1999-00124

**Contract type:** Shared Cost Project

**Total cost:** € 1.219.400

**EC contribution:** € 1.049.400

**Starting date:** 1/02/2000

**Duration:** 36 Months

**Scientific Officer:** Barend Verachtert

**Project website:**

[http://honeybee.helsinki.fi/  
MMKEM/EK/Tutkimus/antho.html](http://honeybee.helsinki.fi/MMKEM/EK/Tutkimus/antho.html)

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## **Functional properties, bioactivities and bioavailability of phytochemicals, especially anthocyanins, from processed foods**

### **BACKGROUND**

The project aims to investigate i) the functional properties (physicochemical, antimicrobial and sensory) of anthocyanin-rich food ingredients and ii) the influence of anthocyanins on parameters related to the aetiology of cardiovascular disease in humans. Novel food processing techniques are used to produce anthocyanin-rich red berry juice for potential nutritional benefits. Anthocyanins, juice, and juice processing by-products will be studied to provide basis for the development of anthocyanin-rich functional food recipes. Molecular mechanisms underlying the biological and physiological effects of anthocyanins and possible confounding factors, hydroxycinnamic acids, are investigated in animal and human liver microsomes and cell lines. The bioavailability and biokinetics of anthocyanins and hydroxycinnamates are confirmed in animal models to a strictly controlled human intervention measuring a wide range of biomarkers.

### **OBJECTIVES**

The project aims to investigate i) the functional properties of anthocyanins and anthocyanin-rich food ingredients and ii) the influence of anthocyanins on parameters related to the aetiology of cardiovascular disease in humans. Novel food processing techniques are used to produce anthocyanin-rich red berry juice for potential nutritional benefits. Anthocyanins, berry juice and berry juice processing by-products will be studied to provide basis for the development of anthocyanin-rich functional food recipes. Molecular mechanisms underlying the biological and physiological effects of anthocyanins are investigated in animal liver microsomes and cell lines. The bioavailability and biokinetics of anthocyanins are confirmed in animal models prior to a strictly controlled human intervention measuring a wide range of biomarkers.

### **(EXPECTED) RESULTS AND ACHIEVEMENTS**

- Improved techniques to increase the phenolic content in red berry juice
- New biomarkers for important food components and their biological effects to be useful beyond the present project
- New anthocyanin-rich functional food recipes
- New insight into the biological and preventive actions of dietary anthocyanins in relation to heart disease
- Applications
- Production of red-berry juices as a healthy alternative to red wine as a dietary protection against cardiovascular disease
- Optimum use of anthocyanins as natural food ingredients and food additives (colorants) with low systemic toxicity
- Development of anthocyanin-rich functional foods by utilising fruit and vegetable by-production

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QLK1-1999-00124: Functional properties, bioactivities and bioavailability of phytochemicals, especially anthocyanins, from processed foods

## European research on functional effects of dietary antioxidants EUROFEDA

**Contract number:** QLK1-1999-00179  
**Contract type:** Concerted Action  
**Total cost:** € 574.076  
**EC contribution:** € 574.076  
**Starting date:** 1/02/2000  
**Duration:** 36 Months  
**Scientific Officer:** Rosanna d'Amario  
**Project website:**  
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## European research on functional effects of dietary antioxidants

### BACKGROUND

Research on the functional role that dietary antioxidants play in promoting health by minimising damage to cells from oxidative damage is as yet uncoordinated in Europe. The project will coordinate this research by:

- European Network for the coordination and exchange of information on the functional effects of antioxidants in food,
- prioritising research tasks to stimulate coordination of future research,
- disseminating outputs to end users.
- These objectives will be achieved through a series of task group and plenary meetings which will review:
  - measurement methods of DNA damage and repair,
  - data on antioxidants bioavailability,
  - their effects on gene expression,
  - their possible role in limiting the decline in mitochondrial efficiency with age. This will be achieved through a series of meetings, conferences, publications and dissemination events targeted at end users.

### OBJECTIVES

- Set up a European research network to exchange information on the results of research into the functional effects of antioxidants present in foods
- Identify the research that will be necessary to fill gaps in knowledge about their effects on health
- Encourage proactive research collaboration between scientists working on different aspects of the functional effects of antioxidants
- Disseminate the information that is obtained to end users in the scientific community, consumer groups, legislators and the food industry.

### (EXPECTED) RESULTS AND ACHIEVEMENTS

The project will produce a series of reviews that describe the current knowledge about the possible role that reactive oxidative species (ROS) play in the initiation of disease and the process of ageing. The potential for dietary antioxidants to reduce the damage caused by oxidative stress will be assessed, the gaps in knowledge identified and priority research goals defined.

The project will:

- Review the known effects of antioxidants at the molecular, cellular, tissue and whole body level;
- Review the reliability and reproducibility of the general and gene-specific methods which have been used to determine oxidative damage and its repair, and the strength and weaknesses of existing biomarkers to measure this damage;
- Exchange information on the 'true' bioavailability of antioxidants;
- Evaluate the data that are available on the effects of antioxidants on gene expression at nutritionally relevant levels of intake;

- Review the data that are available on the effects of antioxidants on mitochondrial function; and
- Analyse the evidence that links specific functional events that result from ROS production and how antioxidants could influence the process.

A series of working groups will be set up and their outputs considered at a plenary meeting. The project will culminate in the organisation of an international meeting on the functional effects of antioxidants. The results of this work will be widely disseminated.

## APPLICATIONS

The growing evidence that ROS generation is responsible for the onset of a wide range of diseases of ageing, and that the processes involved can be ameliorated by dietary factors, places this area at the forefront of the Quality of Life and Living Resources Key Action. The need to encourage relevant research to establish how the onset of diseases such as coronary heart disease, cancer, cataract, and neurological dysfunction as a result of ageing, might be slowed down could have a profound impact on the health budgets of many EU Member States. In addition the project should encourage research which will assist industry to respond to the desire by consumers to eat healthily through the development of novel food products based on sound functional claims. In addition it will assist regulators and the legislative process to regulate products on the market that purport to be effective as dietary supplements and make claims that are not soundly based.

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QLK1-1999-00179: European research on functional effects of dietary antioxidants

# Evaluation of the safety and efficacy of iron supplementation in pregnant women

## FEMMES

**Contract number:** QLK1-1999-00337  
**Contract type:** Shared Cost Project  
**Total cost:** € 2.640.635  
**EC contribution:** € 1.728.065  
**Starting date:** 1/02/2000  
**Duration:** 36 Months  
**Scientific Officer:** Rosanna d'Amario  
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## Evaluation of the safety and efficacy of iron supplementation in pregnant women

### BACKGROUND

Iron deficiency is common and can have harmful effects on the mother and her foetus. Anaemia, therefore, is always treated with iron supplements. However, the levels given vary widely and there is growing concern about the risks associated with overload. Since Fe can generate free radicals, and interact with other nutrients, assessment of supplementation in pregnant women is essential. Volunteers will be given two levels of Fe, within the range given clinically, or a placebo, and the effect on parameters such as oxidative stress, cardiovascular well-being, zinc and copper metabolism, will be measured. We will study treatment directly in patients with ileostoma, identifying the cause of GI upset. We will measure the effect on babies at term, on placental function and on expression of different genes in tissues in supplemented rats and in cultured cells, to elucidate the molecular basis of the changes and a rational basis for supplementation.

### OBJECTIVES

Iron deficiency during pregnancy is common and can cause harmful effects on the mother and her developing child. Consequently, supplementation with iron is recommended if a mother's iron levels are even slightly lower than recommended. The amount prescribed, however, varies widely and there is growing concern about the risks associated with excessive iron accumulation. This project, therefore, will examine the effect of two doses of iron supplements, given within the clinical range, on a variety of indicators of health and well being in pregnant women. Concurrently, we will study the effects of supplementation directly in humans and will test the mechanisms involved using cell culture and animal models.

### (EXPECTED) RESULTS AND ACHIEVEMENTS

We will identify the optimum levels of supplementation during pregnancy and will also determine the maximum safe level. Iron supplements have unpleasant side effects and our data will provide information why this should be the case. Supplementation will have effects on the metabolism of other nutrients in addition to iron, and our experiments will not only demonstrate which nutrients are affected but will also show the mechanisms of the interaction.

In order to prescribe sensible levels of iron, we need a clear understanding of the effect it has on the metabolism of other nutrients. For example, we have preliminary data, which suggest that increased iron levels decrease copper concentrations in the blood. What effect this may have on the developing foetus is not clear. Further, we know that iron is capable of generating free radicals, which may have local toxic effects on the gut lining.

At the molecular level, iron regulates the expression of many genes. Only some of these have been characterised. We will use modern techniques to identify new genes, to study how supplementation alters their expression and how they are regulated during pregnancy.

Surprisingly, supplementation rarely actually alters iron status of pregnant women. Why this is so is not clear. Our data will provide some explanations, probably relating to turnover of iron and associated micronutrients.

The main application will be in the field of public health. We will be able to provide rational guidelines for supplementation strategies and recommendations for safe levels of supplementation. We expect to recommend that women should take supplements much earlier in pregnancy than is currently the case and that lower levels should also be prescribed, especially in the UK, but possibly also in other European countries.

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QLK1-1999-00337: Evaluation of the safety and efficacy of iron supplementation in pregnant women

## Synbiotics and cancer prevention in humans SYNCAN

**Contract number:** QLK1-2000-00346  
**Contract type:** Shared Cost Project  
**Total cost:** € 1.962.002  
**EC contribution:** € 1.710.325  
**Starting date:** 1/02/2000  
**Duration:** 36 Months  
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## Synbiotics and cancer prevention in humans

### BACKGROUND

By means of various experimental models (chemoprevention, tumour implantation in peritoneum and muscle tissue, Min mice model) it was observed that dietary administration of prebiotics (inulin, oligofructose) significantly reduced the processes of carcinogenesis and tumorigenesis.

With probiotics, too, there are some reports of anticarcinogenic properties. In one experiment it was observed that a combination of pre- and probiotic had synergistic anticarcinogenic activity.

In present biomarker project, it will be investigated whether these food ingredients have the potential to reduce carcinogenesis in human volunteers too.

### OBJECTIVES

The project addresses the important problem of the high rate of colorectal cancer (CRC) in Europe. The main aim is to evaluate whether the administration of synbiotics (a combination of pro- and prebiotics) to the diet of human volunteers can reduce the risk of colorectal cancer. The objective will be achieved by:

1. In vitro studies that will identify the synbiotic combination with the greatest competitive advantage in the colonic ecosystem;
2. Establishing the anticarcinogenic effect of this synbiotic, but also of the prebiotic and probiotics separately, by measuring tumour development in a long term (33w) rat colon cancer model;
3. Refining a range of novel biomarkers for CRC in blood, faecal water and biopsies (tumour vs. healthy tissue);
4. Evaluating in human subjects with a history (operated CRC patients) or predisposition for CRC (polypectomised patients) the potential of synbiotics to reduce the risk for CRC

The results from the project will contribute to the formulation of improved dietary advice for Europeans to reduce their risk for CRC.

### (EXPECTED) RESULTS AND ACHIEVEMENTS

The biomarker network was established: several parameters were evaluated for their use as a CRC biomarker. Currently, mRNA levels of different enzymes involved in the cancer process, in vitro tumour promoting activity and metastatic activity, calprotectin, GST  $\pi$  and cyclo oxygenase 2 activity, DNA damage, short chain fatty acids and several immunological parameters are measured in faeces and faecal water, in biopsy samples and in blood.

The synbiotic composition chosen as a daily dose for the SYNCAN human study was 10 g RAFTILOSE® Synergy 1 (enriched inulin mixture) as prebiotic and two types of health promoting bacteria as probiotic:  $10^{10}$  cfu/g *Lactobacillus rhamnosus* (LGG) and  $10^{10}$  cfu/g *Bifidobacterium lactis* (Bb12).

The dietary interventions have started (placebo and synbiotic). They last 12 weeks in a parallel study design. Blood and faeces are sampled at regular intervals and biopsies

are sampled at the beginning and the end of the intervention period. They are forwarded to the the biomarker network for further analysis

By means of an experimental model in which CRC is induced in rats, the SYNCAN has investigated the biological events. Preliminary results indicate that synbiotic and prebiotic treatment significantly reduce the number of tumours in the rat colon. Faecal, blood and tumour tissue are currently being analysed by the biomarker network in order to obtain understanding of the mechanisms involved in the anticarcinogenic activity of pre- and synbiotics.

The wealth of techniques and methods developed and evaluated during the first year of the SYNCAN project provides a firm basis for examining the mechanisms of colon cancer development and the protection against it by synbiotics in the diet. The biomarkers used could provide novel clinical markers to be used in oncology and further elaborate the understanding of the causes and treatment of CRC.

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QLK1-2000-00346: Synbiotics and cancer prevention in humans

**Garlic and health: The development of high quality garlic and its influence on biomarkers of atherosclerosis and cancer in humans for disease prevention**  
**G.H.**

**Contract number:** QLK1-1999-00498  
**Contract type:** Shared Cost Project  
**Total cost:** € 6.127.412  
**EC contribution:** € 3.939.137  
**Starting date:** 1/02/2000  
**Duration:** 48 Months  
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## **Garlic and health: The development of high quality garlic and its influence on biomarkers of atherosclerosis and cancer in humans for disease prevention**

### **BACKGROUND**

Garlic is generally considered as a crop species which is beneficial for human health. However the mechanisms behind the health beneficial effects of garlic are poorly understood. Furthermore, the knowledge on the formation of health beneficial compounds in garlic is also insufficient for a science based garlic cultivation for pharmaceutical purposes. The aim of this European framework V project is to fill these gaps. This will take place in a unique combined European effort which brings together plant and human health scientists.

The production of garlic (*Allium sativum* L.) in Europe is concentrated in the Mediterranean countries. The price of European garlic is high, especially in comparison with Chinese garlic. This price difference could severely threaten the European garlic growers if there was a free market in Europe for garlic. However, to protect the European garlic growers the European Commission issued in 1993 a regulation that only 12000 tons of Chinese garlic can be imported annually. The main objective of the plant part of the project is to develop methods, through improved seed technology and genetics, which will enable the European garlic growers to meet the internal demand for high quality products and to compete on the international level. Cardiovascular diseases and cancer are by far the leading causes of death and morbidity in the EU. The health cost spent on the treatment of these diseases reaches many billion euros. Garlic has been used for a long time as food with many therapeutic effects. Its beneficial effects are directly linked to its sulphur metabolism. Detailed studies on the mechanisms underlying cancer and cardio-vascular diseases are lacking, especially studies with defined garlic preparations and compounds are poorly found. Therefore the main objective of the health part of the project is the analysis of the role of garlic for the prevention of chronic diseases like atherosclerosis and cancer through cellular, molecular and clinical studies in cells, animals and humans. Specific biomarkers will be identified as indicators for the modulation of these diseases on the cellular and tissue level and in humans as a basis for new intervention studies.

### **OBJECTIVES**

There are two main scientific objectives in this project, firstly to understand and improve the production of garlic bio-active compounds by sophisticated breeding techniques, and secondly to improve the understanding of the role of garlic as diet and as therapy in promoting and sustaining health and preventing cancer and cardiovascular diseases like atherosclerosis through cellular, molecular and clinical studies as safe and low cost therapy and preventive agent. Further, we aim to identify the mechanisms by which garlic interferes with the inflammatory process of atherosclerosis and the development of cancer in cells, animals and humans. Two technological objectives are also pursued for industrial potential applications: garlic mass propagation of elite clones, to enable cropping and processing of high quality products, and the development of new garlic pharmaceutical formulations with improved properties and quality for the therapy and prevention of chronic diseases.

## (EXPECTED) RESULTS AND ACHIEVEMENTS

The project is organised into nine interrelated workpackages (WPs): WP one concerns the evaluation of the gene pool for organo-sulphur traits and fertility and the construction of a core collection; in WP two a reliable genetic transformation system and a mass propagation method will be developed and the sexual hybridisation system studied; in WP three the interaction between genotype and environment will be evaluated; WP four involves the analyses of the biochemistry of the sulphur pathway in garlic; WP five will examine the influence of garlic compounds on the patho-mechanisms of cardio-vascular diseases like atherosclerosis, especially the inflammatory process of atherosclerosis, further the enzymes involved in signal transduction regulating cholesterol metabolism and the action and efficacy of garlic preparations in transgenic mice as models for human-like hyperlipidaemia and atherosclerosis. WP six deals with the influence of garlic on the development of cancer, especially the activation and detoxification of carcinogens and prevention of carcinogen genotoxicity as well as the inhibition of the initiation of hepato-carcinogenesis, the metabolism of garlic compounds in tissues, animals and humans and the signalling pathway of apoptosis induction. WP seven will focus on pharmaceutical aspects of new formulations, especially the analysis of existing products on the market and of formulations and on the development of in vitro dissolution systems and analytical methods for the evaluation of indicative release parameters. Further, the development of improved bio-available formulations and preparation of study medication will be performed. WP eight finally will aim at garlic and its bio-availability and metabolic fate in humans and its activity relating to cancer and atherosclerosis with evaluation of inflammatory and cancer biomarkers.

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QLK1-1999-00498: Garlic and health: The development of high quality garlic and its influence on biomarkers of atherosclerosis and cancer in humans for disease prevention

**Health implications of natural non-nutrient antioxidants  
(polyphenols): Bioavailability and colon carcinogenesis  
POLYBIND**

**Contract number:** QLK1-1999-00505  
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**EC contribution:** € 2.310.407  
**Starting date:** 1/01/2000  
**Duration:** 36 Months  
**Scientific Officer:** Rosanna d'Amario  
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## **Health implications of natural non-nutrient antioxidants (polyphenols): Bioavailability and colon carcinogenesis**

### **BACKGROUND**

Colon cancer kills approximately 75000 Europeans per year and even a modest reduction would significantly benefit the EU both socially and financially. Many studies show an effect of naturally-occurring dietary plant polyphenols (non-nutrient antioxidants) on carcinogenesis. There are large differences in consumption of amount and type of polyphenols between North and South with lower risks associated with the Mediterranean diet. We will obtain urgently-needed data to permit a risk-benefit analysis of the significance of dietary polyphenols in the modulation of colon cancer, and whether there might be justification for dietary modification, the production of supplements and novel foods.

### **OBJECTIVES**

We will study the effect of polyphenols on health indicators: uptake and metabolism, influence on carcinogen metabolism, effect on cell proliferation and colon carcinogenesis. Structure-function and dose-response studies will be conducted by combining molecular, cellular and in vivo experimental systems with suitable biomarkers of exposure and effect. By these means we will obtain urgently needed data to permit a risk-benefit analysis of the significance of dietary polyphenols in the modulation of colon cancer, and whether there might be a justification for dietary modification, the production of supplements, or novel foods, etc.

The objectives are to answer the following most important questions identified in these programmes:

- How are dietary polyphenols metabolised?
- How do polyphenols alter the rates of carcinogen metabolism?
- What are the mechanisms whereby polyphenols affect cell signalling involved in apoptosis and proliferation?
- How do polyphenols modulate early events of colon carcinogenesis?

### **(EXPECTED) RESULTS AND ACHIEVEMENTS**

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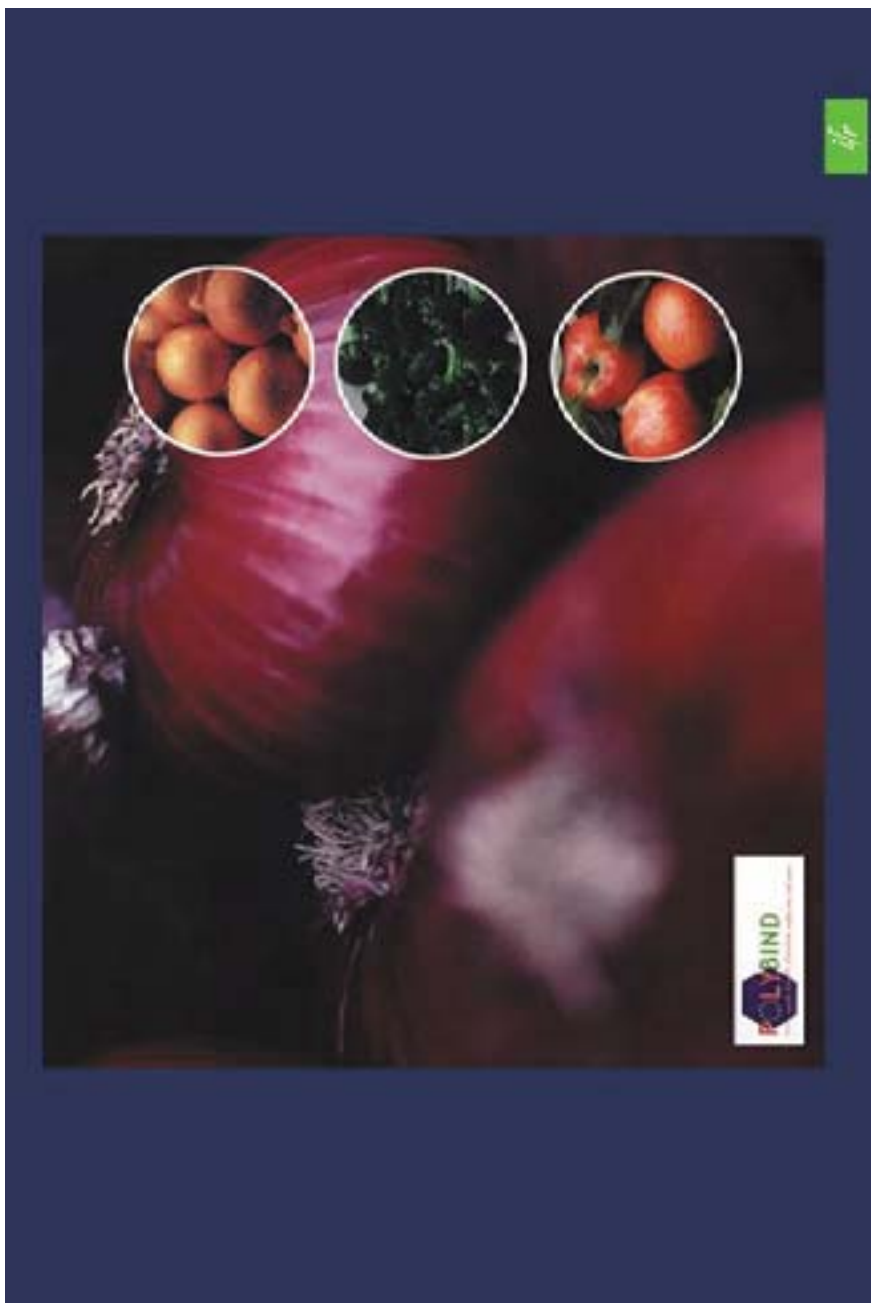
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QLK1-1999-00505: Health implications of natural non-nutrient antioxidants (polyphenols): Bioavailability and colon carcinogenesis

## European Standards Committee on oxidative DNA Damage ESCODD

**Contract number:** QLK1-1999-00568  
**Contract type:** Concerted Action  
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**Starting date:** 1/02/2000  
**Duration:** 36 Months  
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## European Standards Committee on oxidative DNA Damage

### BACKGROUND

Oxidative damage to DNA may contribute to cancer aetiology and is thought to be a factor in ageing. Measurement of 8-oxo-guanine as a marker of DNA oxidation is problematic, and there is an urgent need for standardisation of methods. Spurious oxidation of guanine during sample preparation must be eliminated. This Concerted Action will develop standard protocols and validate methods by distributing standard samples to participants. The final objective will be to reach a consensus on the background level of DNA oxidation in normal human lymphocytes.

### OBJECTIVES

The principal objectives of this Concerted Action are:

- to validate HPLC, GC-MS and LC-MS-MS methods used for measurement of 8-oxo-7,8-dihydroguanine (8-oxo-gua) and 8-oxo-7,8-dihydro-2'-deoxyguanosine (8-oxo-dG) by the use of reference standard DNA samples analysed in parallel in different laboratories, including heavy labelled standards for mass spectrometry;
- to increase the sensitivity and reliability of these 'conventional' methods;
- to measure DNA oxidation in parallel on identical samples using 'conventional' methods and repair endonuclease-based methods;
- to reach a consensus on the average level of oxidation in normal human DNA.

The role of oxidative stress in the aetiology of human disease has recently been recognised. Oxidative changes to DNA are chemically well defined; over 100 modifications have been described, the most abundant being 8-oxo-guanine. This oxidised base is potentially mutagenic; in *in vitro* replication systems, it leads to misincorporation of adenine in the opposite strand. There is some evidence that, at least in animals, the frequency of 8-oxo-guanine in the DNA increases with age. Advanced analytical methods such as GC-MS, HPLC with electrochemical detection, and recently LC-MS-MS have been employed to measure the background level of 8-oxo-gua (8-oxo-dG) in normal human cells. Estimates range over two or three orders of magnitude. An alternative approach, based on the use of a lesion-specific repair endonuclease that introduces strand breaks into DNA at sites of 8-oxo-gua, suggests that the level of damage may be even lower than the lowest of the direct estimates. It is clear that oxidation of gua during sample preparation for GC-MS and HPLC is a serious artefact. Elimination of this problem, standardisation of protocols and reduction of variability and errors in the different assays are essential if we are to achieve a sound judgment of the amount of damage present - a prerequisite for assessing the importance of oxidative DNA damage in the aetiology of diseases such as cancer, Down's syndrome, cystic fibrosis and premature ageing syndromes such as Werner's syndrome as well as its role in normal ageing. This Concerted Action will provide for the systematic exchange of standards and samples between participants, with regular meetings to discuss the results and to optimise methodology. In addition, scientists will take part in exchanges between laboratories to facilitate the adoption of improvements in technique. At each stage, rigorous analysis of the reported analytical results will be carried out, and progress towards the objectives will be very easy to assess.

### (EXPECTED) RESULTS AND ACHIEVEMENTS

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QLK1-1999-00568: European Standards Committee on oxidative DNA Damage

## Diet and cancer: The explanatory value of dietary patterns DIETSCAN

**Contract number:** QLK1-1999-00575  
**Contract type:** Concerted Action  
**Total cost:** € 185.120  
**EC contribution:** € 185.120  
**Starting date:** 1/01/2000  
**Duration:** 36 Months  
**Scientific Officer:** Alkmini Katsada  
**Project website:** not yet available

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## **Diet and cancer: the explanatory value of dietary patterns**

### **BACKGROUND**

Evidence shows that most of the presumably diet-related cancers are not caused (or inhibited) by a single nutrient or food. In order to obtain more insight into the relation between diet and cancer, this study aims to examine the explanatory value of dietary patterns. Dietary patterns reflect the naturally prevailing combinations of nutrients and foods in the free-living population. This study will develop and apply a common methodological approach to examine the relation between dietary patterns and cancer in four European countries, ranging from Finland to Italy. This cross-cultural approach will provide more insight into the validity and generalisability of the dietary patterns, and into the patterns and/or risk factors that consistently enhance or protect against cancer across different countries. This project may contribute significantly to the knowledge on the factors that cause or incite cancer.

### **OBJECTIVES**

This Concerted Action will give insight into the prevailing dietary patterns in each of the participating countries and into the validity and generalisability of the patterns across the countries. Moreover, by linking the dietary patterns found to the risk of several types of cancer in each study, insight will be gained into the patterns and/or risk factors that consistently enhance or protect against these cancers across the different countries.

### **(EXPECTED) RESULTS AND ACHIEVEMENTS**

As dietary patterns are closer to behaviours that can be modified than nutrient intakes, studies on dietary patterns are more constructive for the design of successful nutrition intervention programs. If this project shows that the association between dietary patterns and cancer appears to be universal, dietary patterns are valuable for the development of health promotion activities.

Application, implementation and further systematic development of the methodological approach to analyse dietary patterns is applicable to other epidemiological studies on diet and disease.





QLK1-1999-00575: Diet and cancer: The explanatory value of dietary patterns

## Folate: from food to functionality and optimal health FOLATEFUNCHEALTH

**Contract number:** QLK1-1999-00576

**Contract type:** Shared Cost Project

**Total cost:** € 2.908.990

**EC contribution:** € 2.199.998

**Starting date:** 1/02/2000

**Duration:** 42 Months

**Scientific Officer:** Alkmini Katsada

**Project website:**

<http://www.ifr.bbsrc.ac.uk/folate>

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## **Folate: from food to functionality and optimal health**

### **BACKGROUND**

Folates are currently under intense scrutiny regarding their ability to modulate disease risk, birth defects, CVD/stroke, and possible colon cancer. The objective of this project is to bring together commercial and consumer interests via 7 workpackages which seek to provide folate-rich and enriched foods with specified consumer benefits for optimal bioavailability, function and health. Nutritional scientists, biochemists, clinicians, and food technologists will work together with industry to achieve this objective. Results will include verification of folate efficacy in moderating specific risk factors for chronic disease, quantification of bioavailability of natural folates versus synthetic folic acid added to foods and isolates, and pre-competitive information for development of effective and sustainable dietary strategies to support competitive-edge within the EU food industry, and meet consumer expectations of health benefits.

### **OBJECTIVES**

Folic acid significantly reduces the incidence and reoccurrence of neural tube defects (such as Spina bifida) in women. Marginal folate deficiency is also associated with elevated plasma homocysteine, an emerging risk factor for vascular diseases and stroke, and linked to certain cancers, notably colon. Our understanding of the dose-response relationships in these situations is limited and has led to uncertainties over folate requirements for optimal health and function. Current recommendations suggest that protection from neural tube defects can be achieved through intakes of an extra 400 µg daily of folic acid as supplements, fortified foods or natural food folates. The assumption is that all three routes of administration would have equal effects on folate status.

There is also much debate as to the best means to increase folate intakes in European countries where folic acid fortification is not permitted. Information is required on the relative absorption and utilisation of folates from foods as prepared and delivered to the consumer. The absorption and transport processes of folates from foods are complex and, to large degree, not fully understood. It is not possible to predict bioavailability for a given diet or food, and the influence of food composition and other dietary and physiological variables on folate bioavailability cannot be determined accurately. Understanding factors controlling folate availability is a necessary, pre-competitive step to designing commercial processes, which provide the desired levels of bioavailability and functionality.

There are also concerns as to possible adverse effects, particularly in the elderly, of the high consumption of folic acid from fortified foods, notably masking the diagnosis of vitamin B12 deficiency. Therefore, strategies for increasing the consumption of natural food folates need to be explored. In particular, the question as to whether sufficient quantities can be absorbed from these foods to protect against chronic diseases.

### **(EXPECTED) RESULTS AND ACHIEVEMENTS**

- Development of foods (including improved use of raw materials and optimised food processing techniques) that will enable the diet rich in folates within the range indicated to be protective for human health;
- Verification of the efficacy of folates in moderating specific risk factors for chronic disease;

- Quantification of bioavailability of natural folates versus synthetic folic acid added to foods;
- Pre-competitive information for the development of effective, sustainable, ethically-acceptable dietary strategies for folate-rich foods and folate-enriched products, to support competitive-edge within the European food industry, and meet consumer expectations of health benefits.

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QLK1-1999-00576: Folate: from food to functionality and optimal health

**Functional food against colon cancer:  
Development of a genomics and proteomics based screening assay  
FFACC**

**Contract number:** QLK1-1999-00706  
**Contract type:** Shared Cost Project  
**Total cost:** € 2.897.119  
**EC contribution:** € 1.587.018  
**Starting date:** 1/01/2000  
**Duration:** 36 Months  
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**Project website:** not yet available

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## **Functional food against colon cancer: Development of a genomics and proteomics based screening assay**

### **BACKGROUND**

More than half of the gastrointestinal tract cancers may be related to the diet. Research to identify active components in the diet reducing the cancer risk, to understand the mechanism of cancer prevention and (the last few years) to design functional foods with the specific goal to reduce the incidence of cancers has made considerable progress. However, a systematic search for effective (combinations of) food compounds or ingredients has not been performed, primarily due to lack of good methodology. An (in vitro) bioassay will be developed, based on genomic and proteomic changes in colorectal cells, to assess the efficacy of (functional) food ingredients in prevention or inhibition of the development of early stages of colorectal cancer. The genomic and proteomic changes in colorectal cells will be powerful biomarkers of colon carcinogenesis as a large portfolio of genes and proteins are tested simultaneously and the assays are easy to perform.

### **OBJECTIVES**

The scientific consensus is that cancers are largely preventable, and one of the most effective means of reducing risk is consumption of appropriate diets. Great efforts have been made in the last ten years to identify active components in the diet reducing cancer risk, to understand the mechanism of cancer prevention, to give better dietary recommendation to reduce cancer risk and to design functional foods with the aim to reduce cancer incidences. Two new technologies have recently become available which allow for a thorough assessment of changes in expression of all known genes (genomics) and proteins (proteomics) involved in (colorectal) carcinogenesis. The aim of the present project is to develop a bioassay, based on genomic and proteomic changes in colorectal cells, in order to identify food components specifically designed to prevent the development or progression of colorectal cancer.

### **(EXPECTED) RESULTS AND ACHIEVEMENTS**

The results of the program will contribute to strategies for the prevention of (colorectal) cancer by designing specific functional food ingredients interfering with the onset or promotion of the carcinogenic process.





QLK1-1999-00706: Functional food against colon cancer: development of a genomics and proteomics based screening assay

## Optimal nutrition towards osteoporosis prevention: Impact of diet and gene-nutrient interactions on calcium and bone metabolism

### OSTEODIET

**Contract number:** QLK1-1999-00752  
**Contract type:** Shared Cost Project  
**Total cost:** € 2.044.608  
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## **Optimal nutrition towards osteoporosis prevention: Impact of diet and gene-nutrient interactions on calcium and bone metabolism**

### **BACKGROUND**

The overall objective is to investigate the influence of diet, and its interaction with individual genetic variation, on the metabolism of calcium and bone in postmenopausal women in order to reinforce the scientific base for dietary strategies for osteoporosis prevention in Europe. The project will apply state of the art techniques in human studies to investigate how diet (Na, Ca, protein, vitamin K) and individual genetic variation (genes for vitamin D receptor, Apolipoprotein E) influence metabolic processes of Ca and bone. Four dietary intervention studies will be carried out in postmenopausal women. One of those will also develop and evaluate a novel radio-tracer method for bone loss measurement in intervention studies in humans. Those studies will provide new information on the role of diet and genetic variability in the mechanism of development of osteoporosis and on how dietary strategies may be developed for its prevention.

### **OBJECTIVES**

Overall objective: To investigate the influence of diet, and its interaction with individual genetic variation, on the metabolism of calcium and bone in postmenopausal women in order to reinforce the scientific base for dietary strategies for osteoporosis prevention in Europe.

Specific objectives:

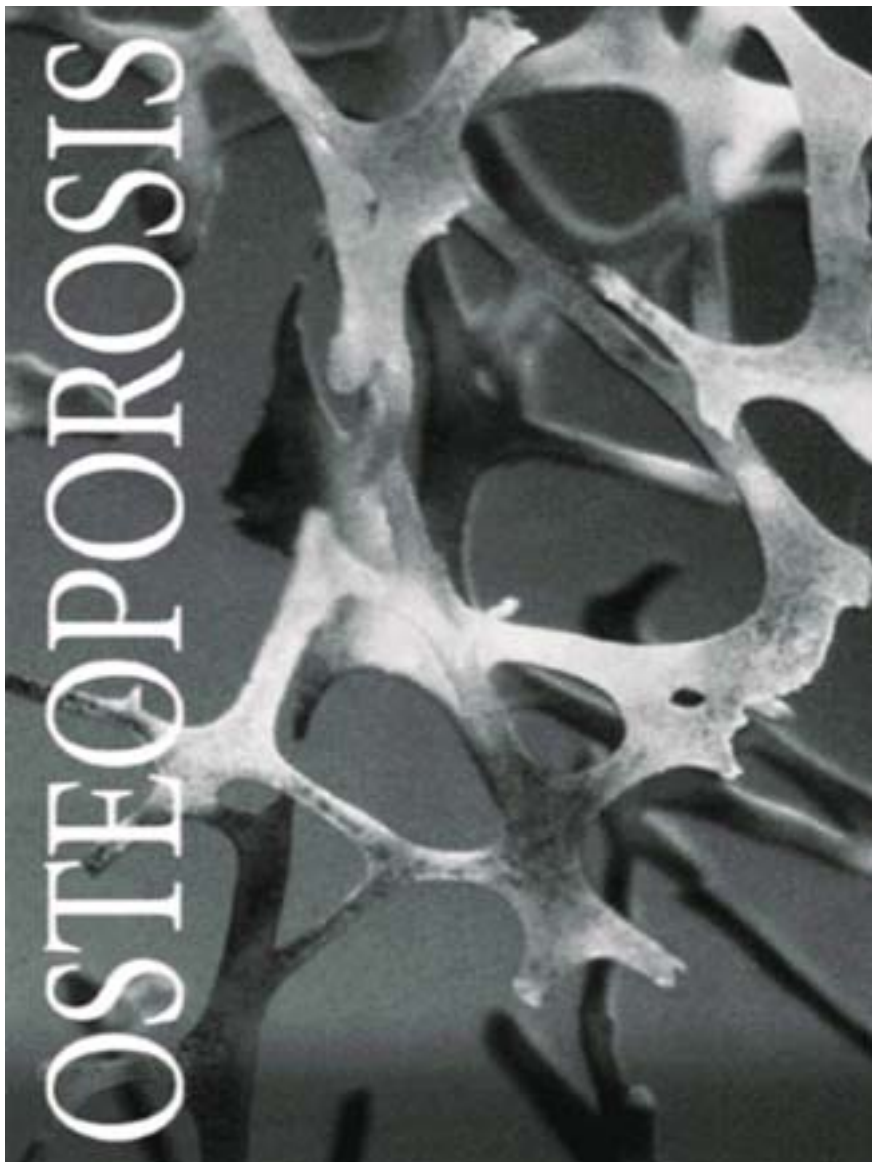
- To determine the effect of a high salt (sodium) diet on metabolism of calcium and bone and how it is influenced by the level of dietary calcium.
- To investigate the effect of individual genetic variation (vitamin D receptor gene) on the adaptive response of calcium and bone metabolism to a calciuric (high sodium-high protein) diet.
- To determine the effect of dietary intake of vitamin K on the metabolism of calcium and bone and how it is influenced by individual genetic variation (apolipoprotein E gene).
- To develop and evaluate a novel radio-tracer ( $^{41}\text{Ca}$ ) method for assessing the impact of diet on bone resorption (loss) and calcium metabolism.

### **(EXPECTED) RESULTS AND ACHIEVEMENTS**

New scientific information on the influence of (i) diet (salt, calcium, protein, vitamin K) and (ii) individual genetic variation on bone integrity and on mechanisms of development of osteoporosis Reinforced scientific base for the development of nutrition strategies, policies and guidelines. Community action programmes and new food products for osteoporosis prevention in Europe. Novel radiotracer method for measurement of bone loss and calcium metabolism in intervention studies in humans. The project will also will contribute to the evolution of EU policy on public health, including women's health, and ageing the attainment of EU social objectives e.g. improvement of the health and quality of life for consumers. The scientific base for improving the quality (particularly the nutritional quality) of food products in response to consumer demands. Will also provide excellent opportunities for the training of European post-graduates and post-doctoral scientists to achieve a high level of expertise in the area of food.

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QLK1-1999-00752: Optimal nutrition towards osteoporosis prevention: Impact of diet and gene-nutrient interactions on calcium and bone metabolism

**Fat-soluble vitamin status and metabolism during ageing:  
Functional and nutritional consequences  
VITAGE**

**Contract number:** QLK1-1999-00830  
**Contract type:** Shared Cost Project  
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## **Fat-soluble vitamin status and metabolism during ageing: functional and nutritional consequences**

### **BACKGROUND**

Among the nutritional factors contributing to maintain health during ageing, fat-soluble vitamins (FSV) are crucial to protect against free radicals-generated deleterious processes or decrease efficiency of the immune system. However, no sound scientific evidence exists to state about specific dietary needs in FSV for the healthy elderly. This project aims at providing such evidence by undertaking studies on male volunteers distributed between 20 and 75 years of age and coming from 3 European countries. Biomarkers and variables related to status, metabolism and functions will be measured either in steady-provide clear information about the physiological characteristics of vitamin A, vitamin E, and carotenoids. Simultaneously, marketing opportunities for FSV-enriched dietetic foods, specifically designed for the elderly will be determined. The scientific and economic evidences obtained in this project will provide basis to implement EU.

### **OBJECTIVES**

The overall objective of this project is to provide clear and sound scientific evidences about the changes in the status, the metabolism and the functions of fat-soluble vitamins (vitamin A, vitamin E, carotenoids), that may occur during non pathological ageing in humans. According to their nature, to their extent, and to their frequency, these age-related changes may or may not result in modifications of the vitamin needs. These vitamins are especially important in the elderly, because of their protective properties: they are needed to maintain an efficient immune status, which is known to fail with ageing. Vitamin E, and probably carotenoids, participate in the oxidant/antioxidant balance and may thus act against free radicals, whose effects are deleterious on many functions affected by ageing.

The knowledge acquired in this project will help to decide whether specific dietary recommendations for these vitamins are required for the healthy elderly. It will also provide a scientific basis for the development of vitamin-enriched dietetic products, specifically designed for this age group.

A secondary scientific objective is to perform geographical comparisons. Three populations, each comprising 100 healthy male volunteers and fulfilling the same inclusion criteria., will be recruited in three European countries, where both the dietary habits and life style are different. Most of the 300 subjects will be assayed for the same analytical or will undergo similar experimental protocols. Although our project is clearly an experimental and not an epidemiological one, it could allow detecting between-country differences in the relationships that we will be seeking to establish between vitamins and ageing.

Beside major scientific objectives, this project has two main technological objectives:

It will provide validation of several methodologies, which have not been used to the same extent so far. This comprises the use of deuterated-labelled vitamins, an approach, which relies on validated techniques, yet has not been used in such a context. This holds also true for the measurements of nuclear receptor in human tissue: these are new attempts to transpose methodologies and techniques developed on animals to human beings.

It will investigate the status, the metabolism and the functions of vitamins in humans, using several biomarkers of exposure and effects, thus providing some basis to validate the less developed biomarkers against the more established ones.

## (EXPECTED) RESULTS AND ACHIEVEMENTS

The expected achievements are:

- a reliable scientific information about the age-effects on the status, the metabolism and the functions of FSV, providing the basis of specific dietary recommendation for FSV intake and status of the elderly.
- a geographical comparison of these effects between three European countries
- a further step towards several methodological validations
- sufficient social and economical information to decide about the feasibility of developing specific FSV-enriched dietetic foods for the healthy elderly.

The results generated in this project will provide a sound scientific basis to implement a nutritional policy towards the elderly, and to develop dietetic foods specifically designed to meet the needs of the healthy elderly population. Dietetic foods differ from ordinary food because of their composition or method of manufacture. Research, development and marketing of a new product category generate high costs, which could not be afforded by most of the manufacturers without the assurance of a wide market. Evidence provided by a multi-centre study will be of major interest for the development of a new and specific food range.

Currently, there is no specific European directive on the specific dietary requirements for healthy elderly people. However, it is clear that healthy elderly can be considered as being in a physiological condition that may benefit from some specially formulated products, which would meet their particular nutritional needs. It is therefore very likely that such products may be marketed. Then relevant scientific work would help national authorities and the European Commission to evaluate the acceptance of these products. If considered necessary, legislation could then be envisaged. Reliable data showing specific nutritional requirements and a real consumer interest for this food category will be of the utmost interest in the elaboration of a directive.

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QLK1-1999-00830: Fat-soluble vitamin status and metabolism during ageing: Functional and nutritional consequences

**Nutraceuticals for a healthier life:  
n-3 polyunsaturated fatty acids and 5-methyl-tetra-hydro-folate  
NUHEAL**

**Contract number:** QLK1-1999-00888  
**Contract type:** Shared Cost Project  
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**EC contribution:** € 2.998.847  
**Starting date:** 1/03/2000  
**Duration:** 42 Months  
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## **Nutraceuticals for a healthier life: n-3 polyunsaturated fatty acids and 5-methyl-tetra-hydro-folate**

### **BACKGROUND**

The project will for the first time undertake a comprehensive, in-depth evaluation of the beneficial roles and interactions of long-chained n-3 polyunsaturated fatty acids (n-3 LC PUFA) and 5-methyl-tetra-hydro-folate (5-MTHF) in cardiovascular health and infant development. It will investigate effects on CVD-related biomarkers and on the development of infants, when mothers had been supplemented during pregnancy. The information obtained will allow the development of various functional foods enriched with stable forms of these nutraceuticals, thereby providing an optimum taste profile and ensuring consumer acceptability. These functional foods will help to reduce the deficit between current intakes of these nutrients and their actual requirement for optimal health in a large proportion of the European population. The products will also be of high commercial value to the European food industry.

### **OBJECTIVES**

The project will for the first time undertake a comprehensive in-depth evaluation of the beneficial roles and interactions of long-chained n-3 polyunsaturated fatty acids and 5-methyl-tetra-hydro-folate in cardiovascular health and infant development. It will investigate effects on CVD-related biomarkers and on the development of infants, when mothers had been supplemented during pregnancy

### **(EXPECTED) RESULTS AND ACHIEVEMENTS**

The information obtained will allow the development of various functional foods enriched with stable forms of these nutraceuticals thereby providing an optimum taste profile and ensuring consumer acceptability. These functional foods will help to reduce the deficit between current intakes of these nutrients and their actual requirement for optimal health in a large proportion of the European population. The products will also be of high commercial value to the European food industry.

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QLK1-1999-00888 Nutraceuticals for a healthier life: n-3 polyunsaturated fatty acids and 5-methyl-tetra-hydro-folate

# Heterocyclic amines in cooked foods: Role in human health

## HC AMINES

**Contract number:** QLK1-1999-01197  
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**Duration:** 36 Months  
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## Heterocyclic amines in cooked foods: Role in human health

### BACKGROUND

Heterocyclic amines (HAs) are formed at ppb level during cooking of meat and fish. Epidemiological studies have shown a correlation between the intake of fried meat and cancer. The carcinogenicity of HAs has been shown in mice, rats and non-human primates. The human risk of HA intake is not clarified, but depends on the level of exposure, dietary factors influencing their uptake and biotransformation, and on the capacity of the individual to handle HAs. Exposure will be determined by new methods for analysis of HAs in foods and for biomarkers of internal and bioactive dose. Endogenous handling will be studied using cloning techniques; critical human enzymes and polymorphisms/genetic susceptibility in the bioactivation and detoxification of HAs and individual DNA repair capacity will be characterised. Exogenous dietary factors modifying the biological handling will be investigated.

### OBJECTIVES

The overall objective is to increase our understanding of the impact of exposure to heterocyclic amines on human health. Three major objectives can be identified: Improvement of (i) the assessments of exposure to HAs, (ii) the understanding of endogenous factors modifying the health effects of HAs, and (iii) the understanding of exogenous (dietary) factors modifying the health effects of HAs.

### (EXPECTED) RESULTS AND ACHIEVEMENTS

Exposure: Analytical methods for the determination of HAs in foods have been optimised and harmonised. Preliminary results of the most popular meat and fish dishes in Austria and in Sweden show that the precursors content in the meat has a marked influence on the formation of HAs during cooking. An analytical method for PhIP in human hair as a long-term biomarker for exposure to HAs has been developed. A metabolite of PhIP, 5-OH-PhIP, was found in urine of exposed rats. Urinary mutagenic activity was measured after ingestion of meat with a defined amount of HAs, and two HAs were identified. The induction of tumours in Min-mice by PhIP has been performed.

Endogenous factors: V79 cell lines that co-express human enzymes have been genetically engineered and used to study the mutagenicity of HAs. Genotoxicity of HAs has been investigated with special emphasis on aminocarbolines in short-term tests. The metabolism of MeA€C has been studied in hepatic microsomes from rats and from humans. The mutagenicity of extracts of fried foods was studied through incubation with *Lactobacillus* strains. Germ-free rats were inoculated with human intestinal microflora and fed a standard or an experimental diet for four weeks to determine the genotoxic response.

Exogenous factors: New genetically altered V-79 cells have been used in two test systems, and it was possible to obtain positive effects with HAs. An improved protocol for the measurement of PhIP-induced DNA damage in mice and rats was established. Effects of Brassica vegetables on IQ induced liver foci in rats were studied; it is possible to use this method to investigate protective effects of vegetables. The effect of Brussels sprouts on urinary mutagenicity, induced by hamburgers, was monitored in a HA sensitive *Salmonella* strain. Preliminary findings showed that the HA induced effects decline after consumption of the vegetables.

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**The role of social, genetic and environmental factors in healthy eating:  
A multicentre analysis of eating disorders and obesity  
FACTORS IN HEALTHY EATING**

**Contract number:** QLK1-2000-00916  
**Contract type:** Shared Cost Project  
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**EC contribution:** € 2.449.635  
**Starting date:** 1/03/2000  
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## **The role of social, genetic and environmental factors in healthy eating: A multi-centre analysis of eating disorders and obesity**

### **BACKGROUND**

This project aims to identify psychosocial and genetic risk factors for anorexia, bulimia and obesity, and correlate these with neuroimaging and neuropsychology. We will create an etiological model for use as tool for improving prevention and treatment of these disorders. We will examine environment by measuring psychosocial and endogenous risk factors such as childhood obesity, sexual abuse, personality and psychopathology. We will examine the human genome for genetic risk factors in large, well-characterised European samples. We will examine the brain by performing by functional magnetic resonance imaging (fMRI) and positron emission tomography (PET) neuroimaging to explore neuroanatomical and neurochemical correlates as well as neuropsychology to reveal cognitive factors that trigger and prolong these disorders. Finally, we will model interactions between psychopathology, genes, culture, gender and psychosocial risk.

### **OBJECTIVES**

The overall objective of this project is to identify psychosocial, cultural and genetic risk factors for anorexia nervosa, bulimia nervosa and obesity, and correlate these findings with functional analysis of the brain in the eating disordered state.

### **(EXPECTED) RESULTS AND ACHIEVEMENTS**

The aim of the first year of research for the HUMAN BRAIN MODULE was to establish the paradigms to be used in the neuroimaging and neuropsychology research during the remainder of the project. Healthy volunteers underwent fMRI while observing pictures related to foods and bodies. The results lead to the hypothesis of direct evidence of sensitivity to disgust in patients with anorexia nervosa. For the neuropsychology paradigms, nine different scales were used. Compared to controls, patients with anorexia showed increased perceptual (CAT BAT) and cognitive rigidity (Uznadze's illusion) and dysdiadokokinesis, whereas bulimic patients showed strong perceptual instability on set flexibility analysis (CAT BAT). Most of these differences were not present in weight recovered anorexics except for cognitive rigidity (Uznadze's illusion), which was seen in fully recovered patients as well, indicating that it is an illness related trait.

The aim of the first year of research for the HUMAN ENVIRONMENT MODULE was to design and translate the questionnaires and recruit volunteers. Besides adaptations and translations of existing questionnaires, two new instruments have been created, validated and translated into the relevant languages of the consortium: the EATATE phenotype interview, a detailed structured diagnostic instrument, and the Modified Risk Factor Interview, an assessment of premorbid risk factors and childhood traits.

The aim of the first year of research for the HUMAN GENOME module was to establish which volunteer patient DNA samples were already available from the participating groups across Europe, to create a list of these available samples and their genotypes, and to perform combined analysis. The existing genotype list and analysis for obesity trios and anorexia nervosa trios were successfully completed and one paper has been accepted for publication.

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**Disseminating the results of EU food research programmes to small  
and medium sized food industries, health professionals and consumer  
groups through a 24-country interactive network system  
FFE IV**

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**Contract type:** Concerted Action  
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**EC contribution:** € 2.562.000  
**Starting date:** 1/01/2001  
**Duration:** 36 Months  
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## **Disseminating the results of EU food research programmes to small and medium sized food industries, health professionals and consumer groups through a 24-country interactive network system**

### **BACKGROUND**

Innovation is an essential precondition for growth, maintaining employment and competitiveness. However, the situation of the European Union in terms of innovation is unsatisfactory, despite some first-rate scientific achievements; this is the “European paradox”. One of the major weaknesses lies in transforming the results of technological research into innovations and competitive. Greater attention needs to be given to dissemination of RTD results and to the expectations of end-users: Small and Medium Enterprises, Health Professionals and Consumers.

### **OBJECTIVES**

Our main objective is to promote innovation in the food sector in Europe and Eastern European countries through the interactive dissemination of RTD results to three target groups: SMEs, Health Professionals and Consumer Groups.

The two specific aims of the Flair-Flow project are:

- the dissemination of results from EU-sponsored food research in a user friendly form to 24 European countries;
- the establishment of a permanent dialog between the scientists and the end-users on topics related to food science: 72 debates will be organised all over Europe.

### **(EXPECTED) RESULTS AND ACHIEVEMENTS**

Flair-Flow will contribute to the new European Research Area (ERA) concept in many ways:

- by using intensively electronic means to disseminate the information to the end-users
- by increasing exchange of scientific information between the 24 countries involved in the project
- by setting up a user-friendly information network focusing on SMEs, health professionals and consumer groups
- by helping Eastern countries to integrate the Flair-Flow network
- by organising debate meetings on food science with European actors.

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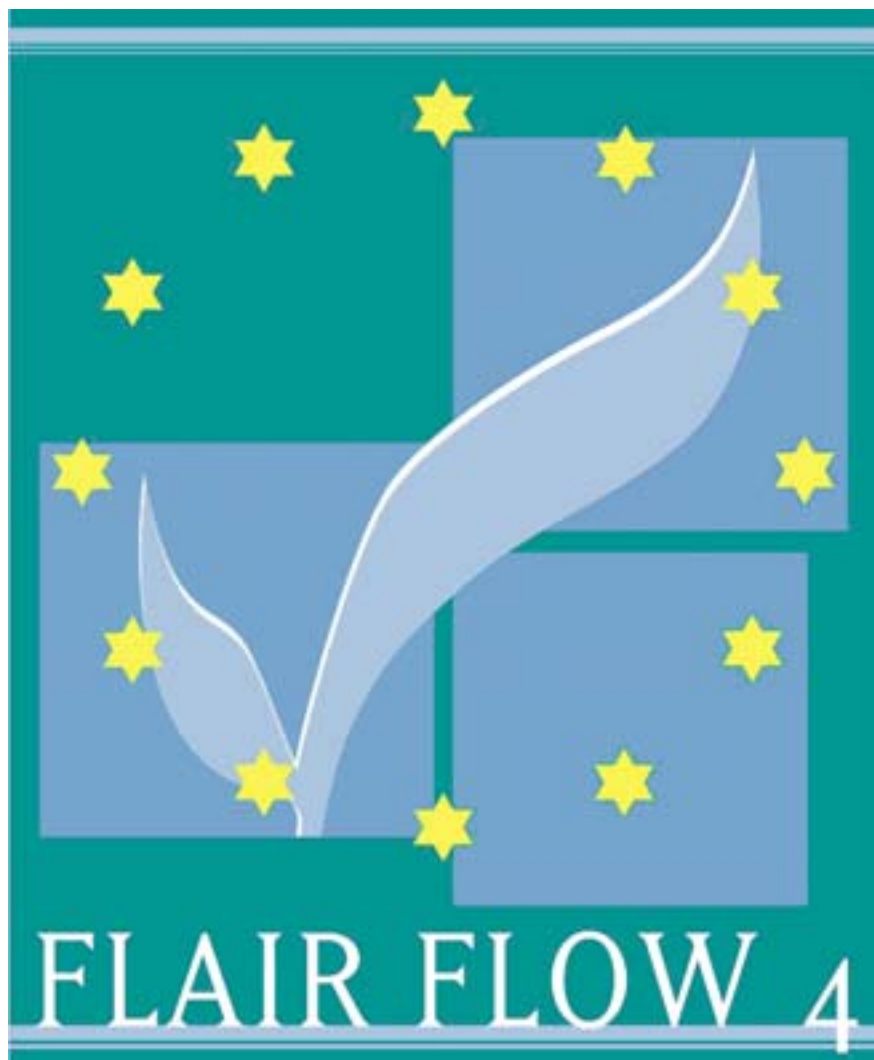
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QLK1-2000-00040: Disseminating the results of EU food research programmes to small and medium sized food industries, health professionals and consumer groups through a 24-country interactive network system

## Hypotensive peptides from milk proteins HTMProt

**Contract number:** QLK1-2000-00043  
**Contract type:** Shared Cost Project  
**Total cost:** € 1.302.936  
**EC contribution:** € 972.781  
**Starting date:** 1/01/2001  
**Duration:** 36 Months  
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## Hypotensive peptides from milk proteins

### BACKGROUND

Milk protein peptides can inhibit angiotensin-I-converting enzyme (ACE). Drugs which inhibit ACE are in widespread use in cardiovascular medicine. Little or no information is available on the physiological efficacy in man of ingesting natural milk protein peptides/hydrolysates which inhibit ACE *in vitro*. Therefore, it is proposed to address this European-wide functional food ingredient problem/opportunity. The proposal objectives are to perform a detailed physiological, physicochemical, immunochemical and cytochemical characterisation, in addition to a consumer assessment of these naturally derived inhibitors of ACE. Milk proteins will be hydrolysed using food-grade proteinases. Clinical/bioavailability trials will be performed in human volunteers. Immunochemical studies will use serum samples from humans fed ACE inhibitory hydrolysates. Cytochemical studies will use human cell culture systems. Consumer awareness will be assessed on a global basis. The outcome of this proposal should lead to the development of clinically validated health claims in respect to the physiological efficiency and safety of ingesting milk protein-derived inhibitors of ACE.

### OBJECTIVES

The long term future and credibility of functional foods depends on the possession of basic scientific data validating beneficial health effect claims of ingesting specific food/food ingredients. Such information, in the case of angiotensin-I-converting enzyme (ACE) inhibitory peptide-mediated control of blood pressure and prevention/treatment of cardiovascular disease is essentially unavailable for chemically well-defined ACE inhibitory peptides/hydrolysates. Therefore, the objectives of this proposal are: (1) to produce and fully characterise a range of ACE inhibitory peptide preparations from milk proteins; (2) to perform functional, cytochemical and immunochemical characterisation on these preparations; (3) to conduct bioavailability/clinical trials using human volunteers on selected physicochemically well-defined ACE inhibitory preparations and (4) to establish the physiological consequences of ingesting such preparations. Furthermore, an integral part of this project is to assess consumer perception/awareness of the potential health benefits of consuming foods/food ingredients containing peptide sequences capable of inhibiting ACE.

### (EXPECTED) RESULTS AND ACHIEVEMENTS

The expected results are:

- The efficient production of peptide/hydrolysate preparations from milk proteins which inhibit ACE.
- The physicochemical, functional, clinical, immunochemical and cytochemical characterisation of ACE inhibitory preparations, and information on the attitude of consumers to ingesting products containing such preparations.
- Development of scientifically validated health claims with respect to the application of well characterised peptide/hydrolysate inhibitors of ACE which provide health benefits in reducing the risk of developing cardiovascular diseases.
- Increased competitiveness for the European food sector.

Applications:

- Potential use of specific milk protein fragments as functional food ingredients to aid in the prevention of specific cardiovascular disease states.





QLK1-2000-00043: Hypotensive peptides from milk proteins

## Functional food, gut microflora and healthy ageing CROWNALIFE

**Contract number:** QLK1-2000-00067

**Contract type:** Shared Cost Project

**Total cost:** € 2.297.775

**EC contribution:** € 1.824.962

**Starting date:** 1/02/2001

**Duration:** 36 Months

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## **Functional food, gut microflora and healthy ageing**

### **BACKGROUND**

Elderly people represent an increasing fraction of the European population. Their higher susceptibility to degenerative and infectious diseases lead to rising public health and social concerns. Appropriate preventive nutrition strategies can be applied to restore and maintain a balanced intestinal microflora exerting protective functions against the above disorders. The project is based on the application of selected biomarkers in hypothesis driven human studies. We will identify the structural and functional specificity of the elderly's intestinal microflora across Europe. Using this baseline information, we will investigate functional food based preventive nutrition strategies aiming to beneficially affect the functional balance of the elderly's intestinal microflora. Expected outcomes include nutritional recommendations as well as new concepts and prototype functional food specifically adapted for health benefits to the elderly population.

### **OBJECTIVES**

The overall objective is to improve the quality of life of the elderly throughout the third age, with emphasis on the preservation of the period of independence recognised as "the crown of life". The focus is on preventive nutrition and the application of functional food to derive health benefits for the ever-increasing European elderly population. Based on hypothesis driven human studies, the specific objectives of the project are 1) to assess structural and functional alterations of the intestinal flora with ageing and across Europe; and 2) to validate functional foods based preventive nutrition strategies to restore and maintain a healthy intestinal flora in the elderly. Implementations include nutritional recommendations as well as new concepts and prototype functional food specifically adapted for health benefits to the elderly population.

### **(EXPECTED) RESULTS AND ACHIEVEMENTS**

- Assessment of the gut microflora diversity and composition in the European elderly, and identification of its alterations with ageing (baseline human study);
- Assessment of modulation of the intestinal microflora (intervention human study with functional food), and potential health benefits towards degenerative pathologies and infectious diseases;
- Improved health status of the ageing population via specific nutritional recommendations;
- Nutritional guidelines based on the complete assessment of a synbiotic product;
- Design and provision of adapted food supplements directed towards intestinal microbial function;
- Validation of processes and rationale for the design of a new generation of functional foods to satisfy health benefits for the elderly, based on innovative technologies.

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QLK1-2000-00067: Functional food, gut microflora and healthy ageing

## Dietary caffeine, health and quality of life in Europe CAFFEINE AND HEALTH

**Contract number:** QLK1-2000-00069  
**Contract type:** Shared Cost Project  
**Total cost:** € 1.449.042  
**EC contribution:** € 1.449.042  
**Starting date:** 1/01/2001  
**Duration:** 36 Months  
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## **Dietary caffeine, health and quality of life in Europe**

### **BACKGROUND**

Although caffeine is consumed daily by more than 300 million EU citizens, its overall impact on quality of life remains unclear. Accordingly, the aim of this project is to characterise the effects of dietary caffeine as consumed in coffee, tea, soft drinks and chocolate. The project, the most comprehensive study of its type undertaken anywhere in the world, brings together a large multidisciplinary team of scientists and consumer organisations. The project will include: (a) basic and applied experimental studies of the effects of caffeine on physiological processes, and physical and mental functions; (b) epidemiological studies of health and well-being in caffeine consumers; and (c) a pan-European programme of information dissemination to consumers, government and industry.

### **OBJECTIVES**

The key objective of this project is to characterise the effects of dietary caffeine, as consumed in coffee, tea, soft drinks and chocolate. The project will include: (a) basic and applied experimental studies of the effects of caffeine on physiological processes, and physical and mental functions, and (b) epidemiological studies of health and well-being in caffeine consumers. In addition, the project will include a component aimed specifically at the dissemination of the scientific findings to consumers throughout EU Members States, government and to industry. The general aims of this project are to (a) obtain better understanding of caffeine and its effects; (b) redress major shortfalls in current knowledge regarding the impact of dietary caffeine on the quality of life of EU citizens, especially in relation to health and wellbeing; and (c) disseminate the findings to all relevant interested parties.

### **(EXPECTED) RESULTS AND ACHIEVEMENTS**

The project will clarify the implications of dietary caffeine for the health and wellbeing of 300+ million EU citizens who consume caffeine daily. Findings will be published as scientific papers and presented at scientific meetings throughout the 36-month life of the project, and will be disseminated in forms that are accessible and meaningful to all interested parties, including consumers, the public media, relevant health authorities, policy makers, and manufacturers of caffeine products.



Caffeine



Coffee



Tea



Cola



**Early malnutrition and programming of adult degenerative diseases:  
Experimental, epidemiological and preventive studies  
NUTRIX**

**Contract number:** QLK1-2000-00083  
**Contract type:** Shared Cost Project  
**Total cost:** € 2.603.557  
**EC contribution:** € 1.952.035  
**Starting date:** 1/03/2001  
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## **Early malnutrition and programming of adult degenerative diseases: Experimental, epidemiological and preventive studies**

### **BACKGROUND**

Higher life expectancy and changing lifestyles have led to an increasing incidence of chronic illnesses such as obesity, diabetes, and cardio-vascular diseases. The key to reduce the burden of these degenerative diseases on society and improving the quality of life of the individual may be in improving the nutrition of the unborn child. Indeed, foetal growth is a complex, dynamic process depending on a continuous supply of nutrients from the mother. Epidemiological and experimental data reveal that deficient foetal nutrition, even over a brief period of time, may lead to irreversible changes in the offspring and to degenerative diseases in adulthood. This programming not only results from malnutrition due to poverty and social deprivation, but also from nutritional imbalances in affluent populations.

### **OBJECTIVES**

The aim of NUTRIX is to provide the scientific basis to the concept of foetal origin of degenerative diseases such as glucose intolerance, diabetes, obesity, hypertension and cardiovascular diseases, at the physiological, cellular and molecular level, and to identify key nutrients required for normal foetal development. This project will combine human and animal studies and focus on the insulin-producing cells, fat cells, liver cells and smooth muscle cells. Ultimately, we aim to formulate nutritional recommendations to pregnant and nursing mothers to improve long-term quality of life and to propose preventive and therapeutic nutritional supplements.

The objectives are to

- Better understand how nutrition of the pregnant and lactating mother affects early development by using three animal models of decreasing nutritional deficiency (global food restriction, protein restriction and folate restriction)
- Evaluate the relative importance of nutritional factors versus genetic factors in foetal programming by comparing genetic growth restriction models with the nutritional models
- Establish the link between experimental and human studies
- Identify key nutrients that serve as sensors of dietary deficiency and which, ultimately, may serve for preventive and therapeutic purposes.

### **(EXPECTED) RESULTS AND ACHIEVEMENTS**

The results of this research will be disseminated in scientific publications in peer-reviewed journals and during presentations during local, national and international meetings. We will strive, by the end of the project, to produce a booklet featuring a summary of our results. Based on the latter, it will also propose guidelines for improving and/or supplementing diets. This booklet will be delivered to health care providers (physicians, obstetricians, paediatricians), people taking care of pregnant mothers and their offspring (midwives, social workers) and to public health authorities such as national associations and institutions as well as to representatives of the European Commission.





QLK1-2000-00083: Early malnutrition and programming of adult degenerative diseases: Experimental, epidemiological and preventive studies

## A process for the assessment of scientific support for claims on foods PASSCLAIM

**Contract number:** QLK1-2000-00086  
**Contract type:** Concerted Action  
**Total cost:** € 1.202.333  
**EC contribution:** € 1.202.333  
**Starting date:** 1/04/2001  
**Duration:** 48 Months  
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## A process for the assessment of scientific support for claims on foods

### BACKGROUND

Claims for ‘enhanced function’ and ‘reduced risk of disease’ are only justifiable when they are based on appropriate, validated markers of exposure, enhanced function or reduction of disease risk. A European network will be set up involving experts from academia, representatives of public interest groups, regulatory experts and the food industry to start with, build upon and apply these suggested principles, arising out of the previous EU Concerted Action on Functional Food Science in Europe (FUFOSE).

### OBJECTIVES

- To produce a generic tool with principles for assessing the scientific support for health-related claims for foods and food components which are eatable or drinkable
- To evaluate critically the existing schemes which assess the scientific substantiation of claims.
- To select common criteria for how markers should be identified, validated and used in well-designed studies to explore the links between diet and health

### (EXPECTED) RESULTS AND ACHIEVEMENTS

A multidisciplinary European Network will be set up to critically assess the criteria currently used for the assessment of the scientific support for claims on foods. The project will be addressed by eight “Individual Theme Groups (ITGs)”. Phase One ITGs include: (A) diet-related cardiovascular disease, (B) bone health and osteoporosis, (C) physical performance and fitness, (D) a review of existing schemes in different countries to substantiate the scientific basis for health-related claims. Phase Two ITGs include: (E) insulin sensitivity and risk of diabetes, (F) diet-related cancer, (G) mental state and performance and (H) gut health and immunity. Initially, ‘Phase One’ ITGs will focus on the above-mentioned physiological areas A-C and on the existing schemes (D). The reports of the four ITGs will be presented in the Plenary meeting and the Plenary will agree on a first draft set of interim criteria. The reports and the set of interim criteria will be published as Publication I and will be the basis for the discussions of the ‘Phase Two’ ITGs (E-H), who will review how these interim criteria can be used, and which new criteria are needed, in four different physiological areas. The Phase Two reports will be presented in the Second Plenary meeting and the Plenary will agree upon a draft set of wider interim criteria. This set of wider criteria will then be published together with the reports of ITG E to H as Publication II. A Consensus Group will use the Publication Packages I and II to propose draft consensus criteria for the scientific support for health related claims for food and food components. These will be reviewed and agreed by the Third Plenary Meeting and published in the PASSCLAIM Consensus Document, Publication III, which will be widely disseminated among the scientific, industrial, regulatory and consumer communities.

The project will impact on measures to improve the quality of life and health by providing consensus criteria, which will assure the validity of health effects and claims on foods for the population as a whole and for particular ‘at risk’ sub-groups. Harmonisation of the science base for health claims will lead to facilitation of the development of new food sources, ingredients or products. Agriculture will benefit because of nutritionally ‘improved’ products returning value to the producers. A common acceptance

of the science base throughout all member states will improve the cohesion in the Union and will contribute to free trade of foods. An improved approach to the scientific support for claims on foods will enhance consumer confidence. Claims could help consumers to make a wise selection of appropriate amounts of foods, based on functionality, and therefore could help to contain healthcare costs. By using the generic tool for the scientific support for the functional properties used as the basis for health-related claims for foods and food components, industry and regulators can benefit from the more effective and economical use of scarce scientific resources.

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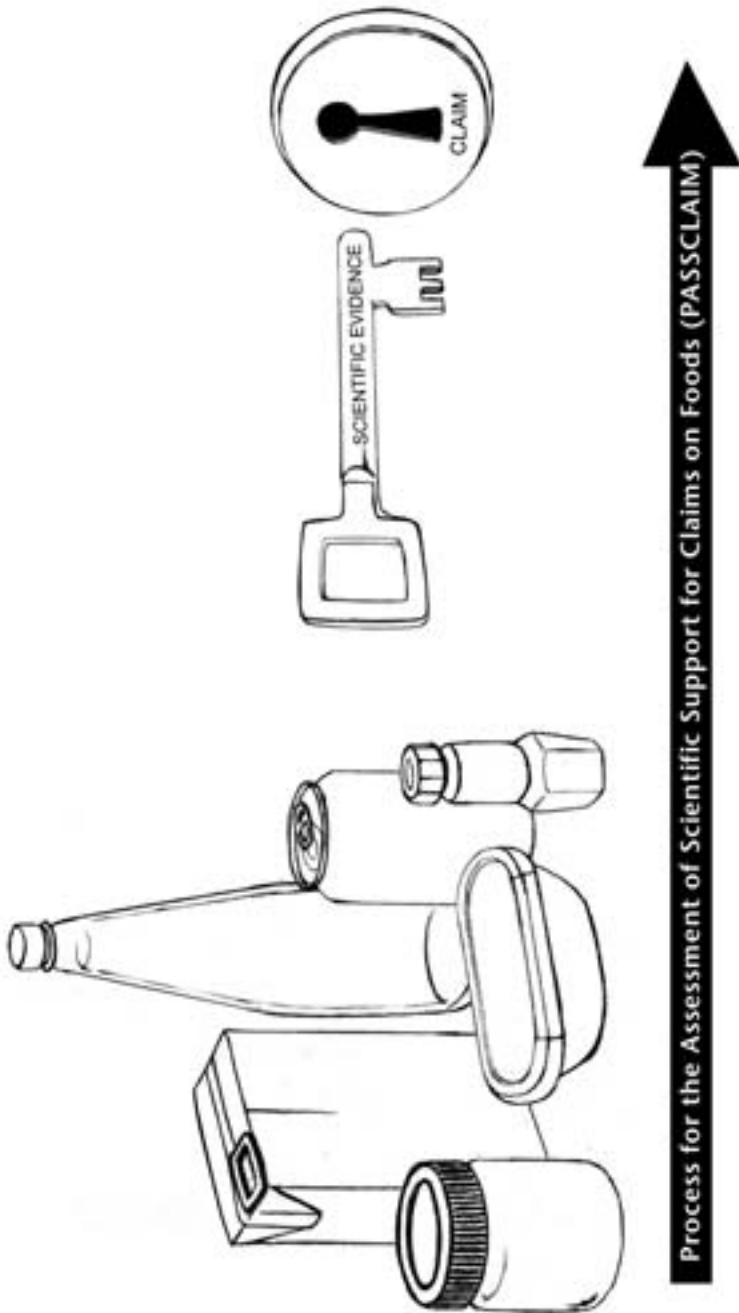
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QLK1-2000-00086: A process for the assessment of scientific support for claims on foods

**Dietary habits profile in European communities with different risk of myocardial infarction: The impact of migration as a model of gene/environment interaction**  
**IMMIDIET**

**Contract number:** QLK1-2000-00100  
**Contract type:** Shared Cost Project  
**Total cost:** € 2.280.625  
**EC contribution:** € 1.587.543  
**Starting date:** 1/01/2001  
**Duration:** 36 Months  
**Scientific Officer:** Barend Verachtert  
**Project website:**  
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## **Dietary habits profile in European communities with different risk of myocardial infarction: The impact of migration as a model of gene/environment interaction**

### **BACKGROUND**

Risk factors influenced by both nutrition and genetic polymorphisms will be studied in 3 European communities by general practitioner's networks. Firstly, 270 Be/Be couples in Belgium will be compared with 270 age- and sex-matched It/It couples in Italy and 270 UK/UK couples in the UK. Migration of Italians to Belgium will be used as a model of interaction between nutrition and genetics, to explain differences in the prevalence of cardiovascular risk across Europe. For this purpose, 270 mixed couples, formed in Belgium by a It/Be marriage, with the same range of age of the It/It, Be/Be and UK/UK couples, will be recruited. Members of the mixed couples will be compared between them and with It and Be couples. A new multilanguage food frequency questionnaire (FFQ) will be developed to evaluate dietary factors and analysed with an adapted program, using integrated tables of food composition.

### **OBJECTIVES**

The general aim is to evaluate the impact of dietary habits on the risk profile of 3 European communities at different risk of myocardial infarction (MI). As an index of MI, risk factors under the combined influence of both dietary and genetic determinants will be studied. These include coagulation factor VII (FVII), homocysteine metabolism and a number of metabolic factors of the so-called "metabolic syndrome" of cardiovascular risk (high blood pressure, abdominal fat accumulation, hyperinsulinaemia/insulin resistance, lipid and lipoprotein abnormalities). Migration from Italy to Belgium will be used as a "natural" model of gene/environment interaction.

Specific objectives will include the evaluation of:

- differences in the variables studied in populations at different risk of MI and host countries for possible future immigrations;
- changes in dietary habits and biomarkers of food intake of mixed couples as compared with those of the original population;
- the effects of such changes on specific CAD risk also in relation to their genetic determinants.

This study will provide:

- an integrated multilanguage questionnaire for food intake assessment to evaluate dietary habits in multicultural populations;
- educational support for health care providers and promotion of healthy dietary habits for the prevention of CAD.

### **(EXPECTED) RESULTS AND ACHIEVEMENTS**

- Assessment of differences in dietary pattern among three European populations at different risk of CAD, changes attributable to migration, evaluation of the possible impact of changing lifestyle on specific indicators of cardiovascular risk, in relation to genetic background;
- Identification of subgroups of subjects exposed to specific environmental or genetic situations which could benefit of "healthy foods" consumption;
- Development and validation of an integrated dietary questionnaire.

The main target of the project will be European General Practitioners who will be involved in scientific and educational programme addressed to their patients. A secondary target is represented by agro-food companies. The dissemination will be addressed to a specialised public (scientists, GPs), through scientific papers, while presentations, articles, conferences and booklets based on the information gathered will be produced for the general public (people, SMEs, policy makers).

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QLK1-2000-00100: Dietary habits profile in European communities with different risk of myocardial infarction: The impact of migration as a model of gene/environment interaction

**Development and application of high throughput molecular methods  
for studying the human gut microbiota in relation to diet and health  
MICROBE DIAGNOSTICS**

**Contract number:** QLK1-2000-00108  
**Contract type:** Shared Cost Project  
**Total cost:** € 2.241.834  
**EC contribution:** € 1.580.229  
**Starting date:** 1/01/2001  
**Duration:** 48 Months  
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## **Development and application of high throughput molecular methods for studying the human gut microbiota in relation to diet and health**

### **BACKGROUND**

The microbial gut ecosystem has a major impact on the health and well-being of humans. Since the makeup and the activity of the gut microflora is highly influenced by diet, the project is designed to better understand the impact of the gastrointestinal microflora on human health and to provide easy-to-use methods for monitoring the gut microflora. Novel methods are to be developed to understand and exploit the nutrition-driven impact of the human gut microflora on health. Since the presently used methods for microflora analysis are time consuming and tedious, high throughput methods for the automated detection of fluorescence-labelled cells based on microscopic image analysis, flow cytometry and DNA arrays will be developed. In situ detection methods for monitoring bacterial gene expression at the cellular level will be developed to monitor the impact of dietary constituents on the transcription of bacterial genes. Samples from human populations will be analysed with the developed methods to identify important factors of microflora development, composition and activity.

### **OBJECTIVES**

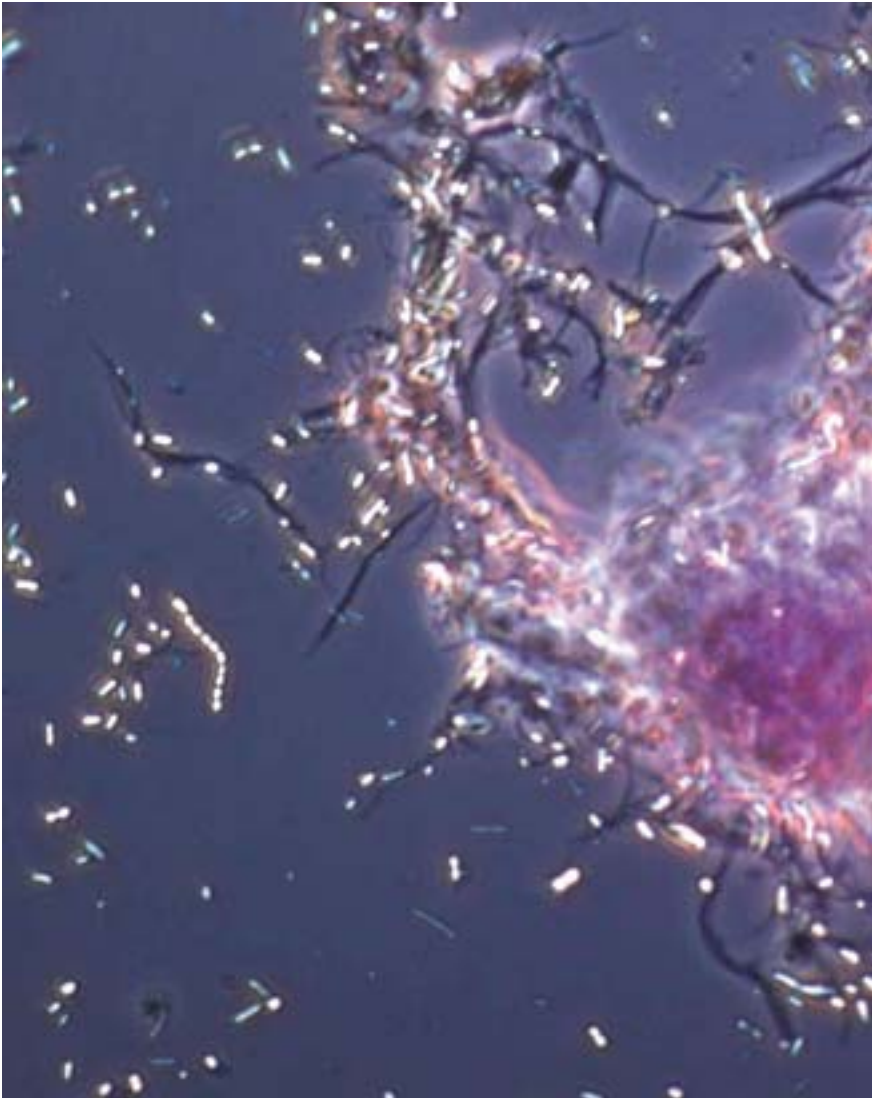
The project is aimed at developing, refining, validating and automating the most advanced molecular methods for monitoring human gut flora composition and bacterial gene expression in selected human populations in response to diet and life style. The specific objectives of the project are (1) to improve and facilitate gut microflora monitoring with molecular methods, (2) to understand antagonistic and synergistic interactions of the intestinal microflora in response to nutrition and (3) to find links between major dysfunctions and the intestinal microflora.

### **(EXPECTED) RESULTS AND ACHIEVEMENTS**

The project is expected to provide methods that allow the rapid detection of intestinal bacteria and their activities. The application of the developed methods will provide baseline data on the intestinal microflora composition in response to origin and lifestyle. The project will also provide fundamental information on biodiversity and phylogeny of the human gut flora. The obtained data will be used to develop a mechanistic concept for diet induced microflora development and to define the role of the intestinal microflora in disease development. The project thereby contributes to investigate the role and impact of food on physiological function, the development of foods with particular benefits, links between diet and chronic diseases and effective communication with the consumer.

The project will provide technological solutions for the rapid detection of gut microorganisms with a high potential for a wide range of applications. The screening of gut flora composition will be applied in relevant biomedical research areas. It will facilitate the diagnosis of a disturbed microflora and the development of rational therapies based on knowledge of disease mechanism. It will support the development of functional foods aimed at improved gastrointestinal function and other health benefits.

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QLK1-2000-00108: Development and application of high throughput molecular methods for studying the human gut microbiota in relation to diet and health

## Probiotic strains with designed health properties DEPROHEALTH

**Contract number:** QLK1-2000-00146  
**Contract type:** Shared Cost Project  
**Total cost:** € 2.234.429  
**EC contribution:** € 1.406.028  
**Starting date:** 1/02/2001  
**Duration:** 36 Months  
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## Probiotic strains with designed health properties

### BACKGROUND

The Lactic Acid Bacteria (LAB) are well-known for their extensive use in the preparation of fermented food products. In addition, the potential health benefits they may exert in humans have been intensively investigated during the last century. However, the mechanisms underlying the health promoting traits attributed to LAB, especially lactobacilli, remain vastly unknown, which has impaired the rational design of probiotic screening methods with accurate predictive value. This project first aims at establishing a correlation between in vitro tests and mouse models mimicking important human intestinal disorders such as Inflammatory Bowel Disease, *Helicobacter pylori*- and Rotavirus-infections. As these diseases correspond to major public health problems, second generation probiotic strains with enhanced prophylactic or therapeutic properties will also be designed during the project. These designed strains and the isogenic parental ones will be used to unravel mechanisms involved in the immunomodulation capacity of specific lactobacillus strains.

### OBJECTIVES

The general purpose of this project is to acquire knowledge about the molecular factors affecting the immunomodulation and/or immunogenicity of selected probiotic lactobacilli so that, in the future, isolates with enhanced protective or therapeutic effect can be screened for or engineered. The objectives of the proposal are on one hand, to unravel mechanisms and identify key components of the immunomodulation capacity of probiotic lactobacilli; and on the other hand, to design “second generation” probiotic strains with enhanced properties against gastro-intestinal disorders.

Two types of gastro-intestinal diseases are targeted: inflammations such as Inflammatory Bowel Disease (IBD) and infections such as those caused by *H. pylori* and Rotavirus. For each of them, “therapeutic” or “prophylactic” (i.e. vaccine) recombinant probiotic strains will be constructed and tested in relevant animal models (i.e. mimicking the human disease) to evaluate their capacity to induce or modulate the immune response in the proper way. This data will be correlated to in vitro testing of the immunomodulation capacity with the hope to identify/develop screening methods that, in the future, will allow isolating efficient probiotic strains targeted to specific applications. Recombinant DNA technology will also be used to assess the importance of specific cell wall components and adhesion factors in immunomodulation.

### (EXPECTED) RESULTS AND ACHIEVEMENTS

Two types of modified probiotic strains will be constructed: mutant strains affected in their cell wall composition and adhesion proteins as well as recombinant strains with enhanced therapeutic or protective properties, focusing on gastrointestinal diseases of inflammatory (IBD) or infectious (*H. pylori* and Rotavirus) origin. The final goal would be to prove that designed probiotic strains could be used as original therapeutic agents as, if successful, they would lead to novel anti-inflammatory treatments or oral vaccines against *Helicobacter pylori* and rotavirus, respectively. It is also expected that, by the end of the study, major progress will have been achieved towards the rational design of simplified probiotic screening methods with accurate predictive value.

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**The role of dietary phytoestrogens  
in the prevention of breast and prostate cancer  
PHYTOPREVENT**

**Contract number:** QLK1-2000-00266  
**Contract type:** Shared Cost Project  
**Total cost:** € 3.328.175  
**EC contribution:** € 2.660.430  
**Starting date:** 1/02/2001  
**Duration:** 36 Months  
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## **The role of dietary phytoestrogens in the prevention of breast and prostate cancer**

### **BACKGROUND**

Cancer in Europe imposes a great social and economic burden; in particular the hormonal cancers, breast and prostate, are major causes of death in the EU. It is now clear that a diet high in plant-based foods may offer protection. This project will analyse the effects of two groups of phytoestrogens (isoflavones and lignans), plant compounds with hormonal activity found in food, on the development of breast and prostate cancer. It will study the metabolism of phytoestrogens, individual variation and its influence on cancer risk. This will also include the development of methods for the discovery of new metabolites and for the rapid measurement of bioactive metabolites. This co-ordinated approach using human patients and volunteers, animal models and in vitro techniques will result in in-depth knowledge of the role of these compounds in the development of cancer and enable informed advice to be available in Europe on the beneficial effects of phytoestrogens in the diet.

### **OBJECTIVES**

The overall aim of the proposal is to investigate the preventive role of phytoestrogens (PE) on breast and prostate cancers and to assess the influence, on cancer risk, of interindividual variation in phytoestrogen metabolism, with special emphasis on metabolites generated by the gut microflora.

This will be addressed by the following scientific and technical objectives

- To isolate and identify new metabolites and develop new methods for the rapid measurement of phytoestrogen metabolites
- To define, using the most recent molecular and analytical techniques, the preventive effects of isoflavones and lignans and their metabolites on the stages of development (initiation, promotion, angiogenesis and metastasis) of breast and prostate cancer.
- To assess the potential cancer-preventing effects of PE in specific transgenic and conventional animal models for the development of breast and prostate cancer.
- To evaluate the importance of oestrogens, oestrogen receptors and PE in the aetiology of breast and prostate cancer by analysis of tissues samples from existing, large-scale breast and prostate cancer patient studies
- To evaluate in a human intervention study the impact of individual variation in the metabolism of phytoestrogens on biological parameters indicative of cancer risk

### **(EXPECTED) RESULTS AND ACHIEVEMENTS**

The following major achievements are expected:

- The isolation and identification of new PE metabolites and food precursors of mammalian lignans and development of quantitative methods.
- The development and validation of new, rapid methods for the detection of the isoflavone genistein and the lignan metabolite, enterolactone in urine. Rapid screening methods for plasma equol and O-DMA (another bacterial product) will also be developed. These will be valuable for other research programmes investigating the activities and health benefits of phytoestrogens
- The studies in animal models, human tissues and in vitro systems will provide crucial information on the ability of phytoestrogens and their metabolites to reduce risk

of prostate and breast cancer. The studies should reveal the likely stages of the carcinogenic process affected and hence provide information on the value of dietary intervention at early, mid and late stages of cancer.

- The human intervention study is expected to provide crucial information on the importance of the metabolic profile of the individual with respect to the cancer preventing activities of PE and will therefore add to the knowledge necessary to make widespread recommendations to the people of Europe as to dietary changes leading to improved health.

This project will contribute to the further technological development of the field in terms of bioassays and evaluation techniques for assessing cancer risk reduction by dietary components and so help maintain Europe's position at the forefront of the this technology.

The rapid methods for detection of phytoestrogens will have applications for the food industry and for researchers investigating aspects of phytoestrogen metabolism and activity in humans. These simple methods will allow an individual to evaluate by her/himself the healthiness of her/his lifestyle.

The successful outcome of the project will also stimulate the awareness of industry and the public of the potential health promoting properties of phytoestrogen-containing foods.

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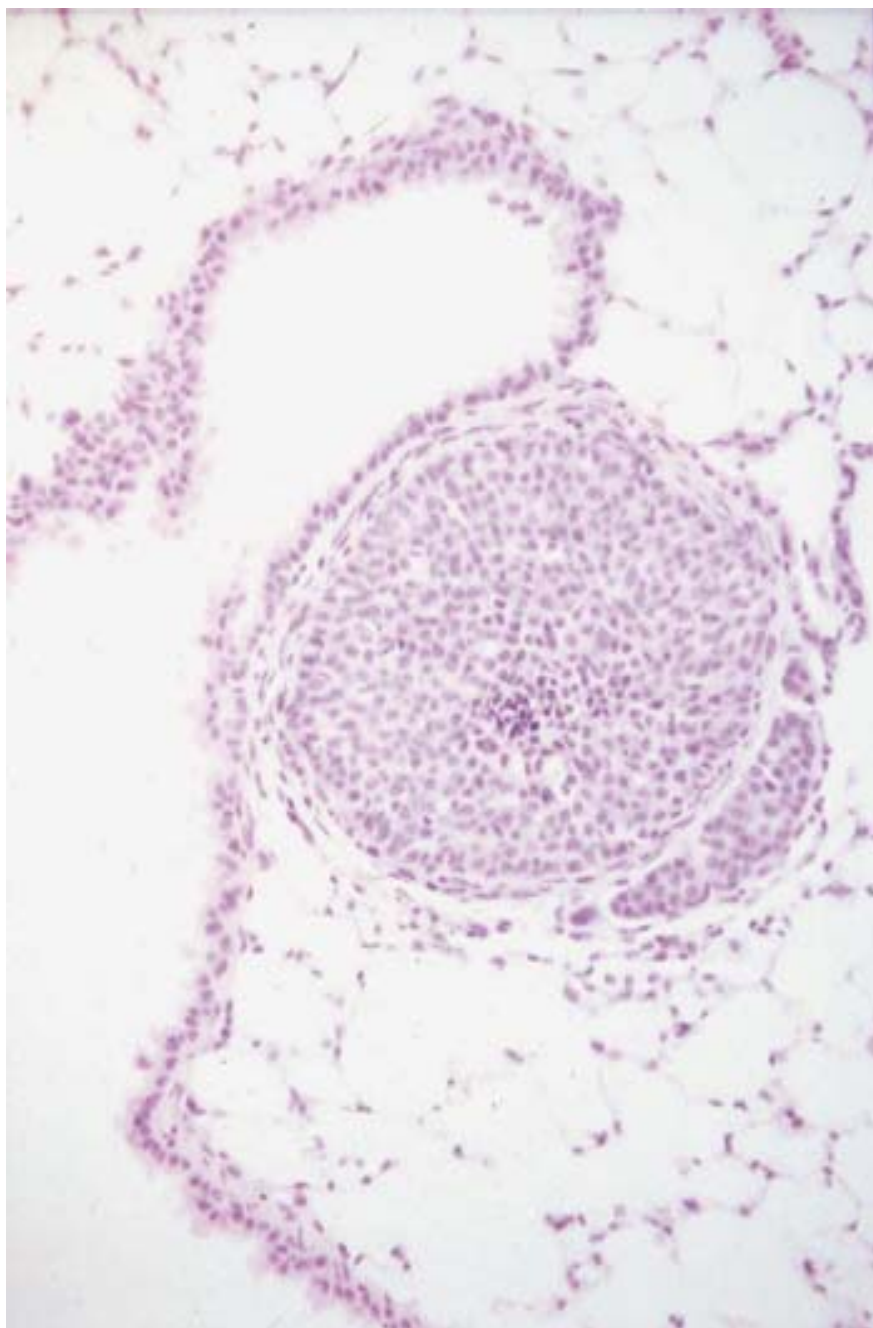
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QLK1-2000-00266: The role of dietary phytoestrogens in the prevention of breast and prostate cancer

# The prevention of osteoporosis by nutritional phytoestrogens PHYTOS

**Contract number:** QLK1-2000-00431  
**Contract type:** Shared Cost Project  
**Total cost:** € 3.382.835  
**EC contribution:** € 1.880.697  
**Starting date:** 1/04/2001  
**Duration:** 48 Months  
**Scientific Officer:** Alkmini Katsada  
**Project website:** not yet available

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## The prevention of osteoporosis by nutritional phytoestrogens

### BACKGROUND

Isoflavones, a subgroup of phytoestrogens mainly contained in soy and soy products, are widely held to have beneficial properties, but the evidence to date is only anecdotal. This proposal addresses the potential role of natural phytoestrogens in osteoporosis prevention among postmenopausal women living in Europe. A one-year large-scale, multicentre, randomised, controlled, intervention trial will be conducted in three European countries using specially-designed isoflavone-enriched foods, combined with rigorous assessments of the changes in bone metabolism. Acceptability of these foods among the target population (women 45 years of age and older) and expectations created by different nutritional claims will be addressed by conducting a survey in five EC state members.

### OBJECTIVES

The overall scientific objective is to provide clear scientific evidence about the effects of soy isoflavones (IF) on bone density and metabolism in Caucasian postmenopausal women living in Europe. IF could be proposed as a potential nutritional alternative to hormone replacement therapy (HRT) on the basis of their partial activity on oestrogen receptors and their bone-sparing effects in oestrogen-deficient animals, but little information exists about their role in preventing postmenopausal bone loss in humans. The knowledge acquired in this project will help to quantify the biological relevance of physiological IF consumption after menopause in osteoporosis prevention. It will also provide a scientific basis to develop IF-enriched foods specifically designed for this age group and to assess optimal IF consumption.

A secondary scientific objective is to perform geographical comparisons on the bone-sparing effects that IF consumption may have after menopause. Three cohorts of 100 women each will be recruited in three European countries where genetic background, dietary habits and lifestyle are substantially different. The knowledge acquired from the above populations will help us to propose an explanatory hypothesis on the epidemiology of osteoporosis across Europe.

The technological objectives of the project refer to IF-enriched food manufacturing and improved IF analysis in food samples and biological fluids:

- Food industries will be provided with valuable information regarding how different manufacturing processes affect the IF quantity and quality of final foods, so that the processing technology can be refined accordingly.
- Delfia-technique (TR-FIA methods) will be validated against GC/MS for equol and ODMA measurements in plasma and daidzein, genistein, equol and ODMA in urine samples. This validation will provide researchers with a valuable tool to assess isoflavones in biological samples, which is easier to perform and less time consuming than HPLC or mass spectrometry techniques.

This project also aims to evaluate the economical relevance of increased dietary IF by:

- a careful estimation of the characteristics of the consumers' audience to which IF-enriched foods will be mainly addressed (women 45 years of age and older).

- an estimate of the cost-effectiveness of IF consumption as an osteoporosis prevention strategy compared to other existing alternatives approved in Europe. This estimation will be based primarily on the results of the main intervention trial.

### (EXPECTED) RESULTS AND ACHIEVEMENTS

- Quantitative information about the effects of dietary IF on bone density and bone metabolism in healthy Caucasian postmenopausal women living in Europe.
- Geographical comparison of these effects between three European countries with different genetic background, dietary habits, and lifestyle for explanatory hypothesis formulation.
- Information on the manufacturing process of IF-enriched foods.
- Information on consumers' perspective on the consumption of IF-rich foods.

### Applications

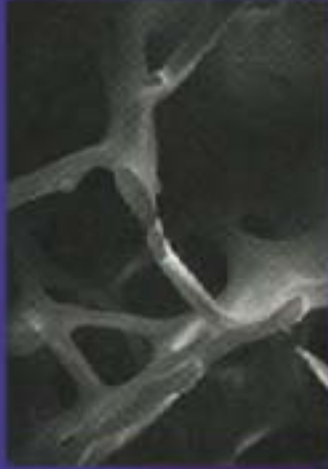
The project deliverables may be used by food industry and regulatory authorities in deciding whether it would be appropriate to undertake large-scale product manufacturing and marketing.

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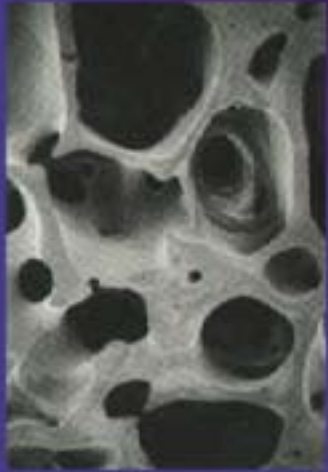
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**Osteoporosis**



**Health**

**Case-only study on the interaction of diet and genetic predisposition  
in the occurrence of breast cancer in young women  
C.O.S.**

**Contract number:** QLK1-2000-00466  
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**Total cost:** € 970.640  
**EC contribution:** € 970.640  
**Starting date:** 1/03/2001  
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## **Case-only study on the interaction of diet and genetic predisposition in the occurrence of breast cancer in young women**

### **BACKGROUND**

The breast cancer (BC) risk of women with germline mutations of BRCA1 or 2 or other high penetrance genes is dramatically increased especially at young ages. Dietary and other modifiable life-style factors, however, may influence the early occurrence of BC in mutation carriers. Fruit and vegetable, vitamin E, soy products and low glycaemic index food, as well as a low index of abdominal obesity, have been suggested to confer greater protection against hereditary BC than against sporadic BC. Mechanistic explanations include hormonal effects of diet and antioxidant protection in women with impaired DNA repair. This CASE-ONLY STUDY aims at testing exposure in patients with and without genetic predisposition, as established through family history or genetic testing. The study base will comprise over 5.000 patients who got BC before the age of 40.

### **OBJECTIVES**

**MAIN OBJECTIVE:** To investigate the interaction between genetic susceptibility and dietary factors in the occurrence of breast cancer (BC) in young women.

**MAIN EXPECTED ACHIEVEMENT:** To establish whether there are perspectives for reducing heritable BC risk through dietary modifications, to quantify their potential effect, and to develop strategies for preventive counselling. Germline mutations of BC genes such as BRCA1 and 2 confer very high lifetime risk of developing BC. Several mutations carriers, however, do not develop BC at all or develop it only late in life. It is reasonable to hypothesise, therefore, that the penetrance of the genetic trait may be regulated through other genetic or non-genetic factors. The confirmation of an association of modifiable environment factors with the penetrance of BC genes would help establishing priorities for preventive trials and would open a new perspective for genetic counselling.

### **(EXPECTED) RESULTS AND ACHIEVEMENTS**

- Establishment of the COS Working Group and election of a Steering Committee
- Agreed protocol and questionnaires
- Data base of patients recruited
- Software for classifying families
- Paper on “Selecting families for genetic susceptibility testing”
- Systematic case-only analyses of gene-environment interactions
- Scientific paper(s) on the effects of diet on the expression of BRCA genes
- Final workshop and planning of further studies.

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**Dietary and genetic influences on susceptibility or resistance  
to weight gain on a high fat diet  
DIET AND OBESITY**

**Contract number:** QLK1-2000-00515  
**Contract type:** Shared Cost Project  
**Total cost:** € 3.416.060  
**EC contribution:** € 2.462.929  
**Starting date:** 1/01/2001  
**Duration:** 36 Months  
**Scientific Officer:** Barend Verachtert  
**Project website:** not yet available

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## **Dietary and genetic influences on susceptibility or resistance to weight gain on a high fat diet**

### **BACKGROUND**

Diet is a major factor in the development of obesity, but its interaction with a susceptible genotype is poorly understood. We will assess the prevalence of high fat consumers (HFC) and phenotype groups that appear to be resistant (DIO-R) or susceptible (DIO-S) to diet induced obesity (DIO). DNA banks from HFCs who are lean or obese and from obese children who consume a HF or LF diet will be screened using candidate genes. A rat model of DIO will be investigated to identify diagnostic biomarkers of DIO-R or DIO-S, and to define the mechanisms involved in defence of obesity. We will also study the influence of foetal and early life nutrition on relevant phenotypes. We will develop a web site to provide accessible information on diet, energetics and genetic predisposition to obesity to a lay audience, in particular obese children and their families.

### **OBJECTIVES**

The overall objective of this project is to identify the causes of weight gain on a Westernised, energy dense, high fat diet, and to apply these findings in the diagnosis, prevention and management of obesity in the human population. This will involve examination of the interaction between diet and genetic background in the susceptibility or resistance to obesity, as well as the genetic basis of dietary preference, and the influence of early life nutrition. The risk factors that define predisposition to obesity and the interaction of diet with this susceptibility (diet-induced obesity) will be investigated. The phenotypes associated with food preference and susceptibility to weight gain and obesity on a high fat diet will be described and the genetic basis of this susceptibility investigated through molecular genetic studies. Diagnostic biomarkers of susceptibility or resistance to excess weight gain on a high fat diet and the mechanistic basis of post-dieting weight gain will be investigated a laboratory rodent model of diet-induced obesity. The effect of early life nutrition on dietary preferences in juvenile or adult life, susceptibility to obesity, and the programming of brain energy balance signalling systems will be investigated in parallel clinical and laboratory rodent studies.

### **(EXPECTED) RESULTS AND ACHIEVEMENTS**

The project will advance our understanding of mechanisms that determine why a high fat diet is preferentially selected by some individuals but not by others, and how genetic background interacts with such diets to confer susceptibility or resistance to obesity. A major outcome will be the detailed description of the phenotype that is associated with susceptibility to weight gain on a high fat diet in both the human population and in the rat model, and the association of genetic markers with these phenotypes in humans. There will be further enhancement of our understanding of the role of maternal nutrition and diet composition on the dietary preferences of children/offspring and their susceptibility to develop obesity. Central nervous system correlates of these characteristics will be described. A web-site will be established, targeted specifically at a lay rather than an academic audience. The multi-lingual site will illustrate the basic relationships between diet, energy expenditure and genetic predisposition in the development of obesity, and will be designed to be appealing to all age groups, but particularly children and adolescents, and will feature 'familiar' cartoon-like characters. The

web-site is intended to be simultaneously entertaining and educational, and will supplement and reinforce conventional media, containing material that will range from accessible summaries of recent research progress to lifestyle and dietary advice.

Applications: Understanding phenotypic variation in susceptibility to diet-induced obesity in the population will help us better understand how to amplify resistant traits in susceptible individuals. An improved ability to diagnose individuals at risk will allow treatment and preventive measures (dietary and lifestyle advice), including advice during pregnancy, to be more targeted. Such an outcome will benefit individuals, the wider community and healthcare providers. Identifying genes involved in the excess consumption of dietary fat, and in the susceptibility to develop obesity on high fat diets could make an important contribution to our understanding of genetic disposition toward common dietary obesity. Detailed mechanistic studies of rodent models will describe the characteristics conferring susceptibility or resistance to obesity, the interaction of voluntary exercise and obesity, and will delineate the mechanisms underlying the defence of obese body weight. These regulatory processes lie at the root of the problems experienced by obese subjects attempting to lose weight by dieting, and this information may form the basis of lifestyle advice for susceptible individuals, or identify targets for pharmacological manipulation.

Despite the current popular concern surrounding early life nutrition, little is known about how nutritional events influence subsequent physiology. Early nutritional experiences have a major influence on body weight and the probability of developing obesity in later life. It is possible that manipulation of the maternal diet during foetal and early neonatal life may alter the 'settings' of brain control systems regulating energy balance. Our hypothesis is that nutrition during critical phases of development could thus contribute to susceptibility to obesity. Such issues are best addressed in laboratory animal models but experimental outcomes will be applicable to the human situation.

As the pace of scientific advance increases there is an increasing need for information relating to obesity to be made available to the lay public in an accessible format. Complex issues are involved in susceptibility to obesity and there is a critical gap in the range of information available to members of the general public, practitioners and the patients, including children. The obesity web-site will fill the gap that exists between obesity web-sites of academic orientation and the popular press.



QLK1-2000-00515: Dietary and genetic influences on susceptibility or resistance to weight gain on a high fat diet

**Design of foods with improved functionality and superior health effects using cereal beta-glucans**  
**BETA-GLUCAN**

<b>Contract number:</b> QLK1-2000-00535	<b>Coordinator:</b>
<b>Contract type:</b> Shared Cost Project	Dr Gunilla Önning
<b>Total cost:</b> € 2.732.830	Lunds Universitet
<b>EC contribution:</b> € 1.905.510	Center for Chemistry and Chemical Nutrition
<b>Starting date:</b> 1/02/2001	Getingevägen 60
<b>Duration:</b> 36 Months	221 00 Lund
<b>Scientific Officer:</b> Jürgen Lucas	Sweden
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## **Design of foods with improved functionality and superior health effects using cereal beta-glucans**

### **BACKGROUND**

Hyperlipidemia and type 2 diabetes mellitus in middle-aged and elderly subjects are becoming an increased burden for the health-care system for European countries. One type of soluble fibre, cereal beta-glucans, has been claimed to be especially active to lower plasma lipid levels and also to improve the glucose tolerance. Thus, cereals rich in beta-glucans may be a useful nutritional tool to better control these metabolic disorders. One problem, however, is that the acceptability of these products is too low for many consumers. This could be improved by offering a wider range of foods enriched in beta-glucans. The major limiting factor for the exploitation of this effect is that presently beta-glucans can only be added in a low amount to foods due to problems with induced changes in viscosity, texture and flavour, which in turn are due to the low purity of available beta-glucan preparations.

### **OBJECTIVES**

The main objectives of the project are:

- To develop methods for the isolation of different types of high purity soluble beta-glucans on an industrial scale from cereals, such as oats and barley;
- To characterise the chemical, physical and sensory properties of the new beta-glucan preparations;
- To evaluate the physiological effects of the new beta-glucan preparations in an animal model and in humans;
- To incorporate the new beta-glucan preparations in new food prototypes;
- To evaluate the consumer acceptance of the new food prototypes;
- To evaluate the physiological effects of the new food prototypes in humans.

### **(EXPECTED) RESULTS AND ACHIEVEMENTS**

- New preparations of beta-glucans from cereals with previously unattained purity and subjected to thorough chemical and sensory characterisation.
- Scientific basis to predict the impact of different beta-glucan preparations on lipid and glucose metabolism in relation to chemical properties.
- Development of a new range of beta-glucan enriched functional food prototypes with good consumer acceptability.

Applications:

- Consumers: Functional foods containing cereal derived beta-glucans to improve the control of hyperlipidaemia and of blood glucose.
- Industry: A new, natural ingredient having scientifically proven 'functional food' properties in the extremely important food-health area.

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QLK1-2000-00535: Design of foods with improved functionality and superior health effects using cereal beta-glucans

**Probiotics and gastrointestinal disorders:  
Controlled trials of European Union patients  
PROGID**

**Contract number:** QLK1-2000-00563

**Contract type:** Shared Cost Project

**Total cost:** € 1.648.353

**EC contribution:** € 1.531.913

**Starting date:** 1/02/2001

**Duration:** 36 Months

**Scientific Officer:** Jürgen Lucas

**Project website:**  
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## **Probiotics and Gastrointestinal Disorders: Controlled trials of European Union patients**

### **BACKGROUND**

Two distinct long-term (one year), large-scale, multi-centered, randomised, double blind, placebo-controlled probiotic-based clinical trials of remission maintenance within a subset of the European Union population suffering from Inflammatory Bowel Disease (IBD) will be performed. In former EC-funded studies, two probiotic bacterial strains have been isolated, characterised and demonstrated to be safe and efficient.

### **OBJECTIVES**

- The efficacy of probiotic micro-organisms, administered as fermented milk products, in maintaining remission of inflammatory bowel disease (IBD) – Crohn’s disease and ulcerative colitis – will be assessed.
- The PROGID partners will establish a repository of biological samples (blood, saliva, and faeces) isolated from a subset of the EU population suffering from Crohn’s disease or ulcerative colitis. This material may provide information from which the effects mediating probiotic effects may be elucidated.

### **(EXPECTED) RESULTS AND ACHIEVEMENTS**

- Assessment of the efficacy of 2 previously-isolated and well-characterised probiotic micro-organisms in the treatment of European patients with inflammatory bowel disease (i.e., Crohn’s disease or ulcerative colitis);
- Critical determination of the role of enteric flora in initiating, or promoting, inflammatory events in the pathogenesis of inflammatory bowel disease;
- Characterisation of the population dynamics of microbial flora associated with inflammatory bowel disease through both conventional microbiological techniques and existing innovative molecular biology-based technologies, which will also identify the major unculturable groups of gastrointestinal microbial flora.
- Determination of the effects of consumption of the two selected probiotic bacteria on the host response.

**Nutrient-gene interactions in human obesity: Implications for dietary guidelines**  
**NUGENOB**

**Contract number:** QLK1-2000-00618  
**Contract type:** Shared Cost Project  
**Total cost:** € 4.011.639  
**EC contribution:** € 3.208.844  
**Starting date:** 1/02/2001  
**Duration:** 36 Months  
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## Nutrient-gene interactions in human obesity: Implications for dietary guidelines

### BACKGROUND

An epidemic of obesity afflicts European populations, posing a major public health challenge due to the associated severe problems and inability to manage them. The project aims at improving understanding of interaction between nutrition (i.e. fat intake) and genetic variations and functions in obesity. Seven hundred and fifty obese and 150 reference subjects will be examined by a scrutiny of dietary habits and relevant life style aspects, a 3-day dietary standardisation at 37% of energy as fat, a 1-day clinical investigation with a test meal with 60% fat, and a 10-week hypocaloric dietary intervention (~ 600 kcal energy deficit per day), either with a low fat content (20-25% fat) or with a high fat content (40-45% fat). Metabolic and hormonal responses to the test meal, changes during the intervention period in body weight and composition, and in gene expression in adipose tissue will be related to genotypes of selected new candidate genes. Such knowledge may improve treatment and prevention of obesity.

### OBJECTIVES

The overall objective of the project is to elucidate the role in human obesity of interactions between macronutrient composition of the diet with particular emphasis on fat intake and specific genetic variants. It aims at combining clinical/physiological variables to the effects of a very high-fat test meal challenge and a long-term hypoenergetic low-fat or hypoenergetic high-fat diet with knowledge of genetic make up and expression levels of individual genes.

This objective can be divided into the following specific aims:

- Identification and characterisation of novel nutrient-sensitive candidate genes for obesity, i.e. genes in which variants result in differential responses in obesity-related physiological functions and in adipose tissue to nutrient challenges such as a high-fat meal and a long-term hypoenergetic alteration of dietary fat content.
- Assessment of the effects of the variants and combinations of variants in known and novel nutrient-sensitive genes on the response in obese subjects to a high-fat test meal in the physiological functions: appetite and satiety, energy expenditure and nutrient partitioning, and circulating obesity-related substrates, hormones and metabolites.
- Assessment of the combined effects the variants of novel and known nutrient-sensitive genes and a short- and long-term alterations in dietary fat content on the differential expression of selected functional genes in adipose tissue.
- Identification of predictors of the changes in body weight and composition of obese subjects during a long-term hypoenergetic low-fat or high-fat dietary intervention programme. These predictors may be: a) variants or combinations of variants of the nutrient-sensitive genes, b) the obesity-related life style factors, c) the differential physiological functions observed at the test meal challenge, d) the gene expression in adipose tissue, or e) gene-phenotype or gene-environment interactions based on combinations of these predictors.

### (EXPECTED) RESULTS AND ACHIEVEMENTS

This project is expected to increase in our understanding of the interaction between dietary fat and the genetic predisposition to obesity. This new knowledge will improve

in several ways the basis for the ability to limit the development of the epidemic of obesity by more effective and more precisely targeted prevention and treatment.

More specifically, the expectation is to achieve more precise knowledge about, and improved understanding of:

- Genomic position and structure, functional variants, and regulation of several novel nutrient-sensitive genes that may be involved in the pathogenesis of obesity.
- The specific mechanisms underlying the well documented genetic predisposition to obesity, which is polygenic and probably heterogeneous with different genes playing a major role in different subsets of obese subjects.
- Genes actively involved in the regulation of metabolic efficiency, in excessive accumulation of fat in adipose tissue and in the changes in fat content of the adipose tissue induced by alterations of the dietary fat content.
- The complex role of fat intake in the pathogenesis of obesity by disclosing the specific nutrient-gene interactions both at a challenge of a single high-fat meal and during a long-term low-fat or high-fat dietary intervention.
- The inter-individual variation in the response to a fat challenge by evaluating the physiological responses to a high-fat test meal in relation to the specific genotypes of the obese subjects, which will characterise the obese subjects with regard to their ability to metabolise fat.
- The inter-individual variation in the changes in body weight and composition during a long-term hypoenergetic low-fat or high-fat dietary intervention.

It is envisaged that the results of this project may lay the grounds for:

- Development of a new obesity taxonomy, in which new modes of classification of subtypes of obesity are based upon their specific genotypes, and the nutrient-gene interaction emerging during the high-fat test meal or the hypoenergetic low-fat or high-fat dietary intervention programme.
- Development of diagnostic tools – on the basis of the genotyping and the responses to the challenge to a high-fat meal – that can discriminate obese subjects with respect to effectiveness of a long-term hypoenergetic low-fat or high-fat dietary intervention allowing accurate targeting of this intervention and delineation of obese subjects in whom other means of intervention are needed.

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QLK1-2000-00618: Nutrient-gene interactions in human obesity: implications for dietary guidelines

## Towards a strategy for optimal vitamin D fortification OPTIFORD

**Contract number:** QLK1-2000-00623  
**Contract type:** Shared Cost Project  
**Total cost:** € 1.754.698  
**EC contribution:** € 1.754.698  
**Starting date:** 1/01/2001  
**Duration:** 36 Months  
**Scientific Officer:** Alkmini Katsada  
**Project website:** www.optiford.org

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## **Towards a strategy for optimal vitamin D fortification**

### **BACKGROUND**

Vitamin D deficiency is known to be very common in the elderly. It represents a major public health problem as it is recognised to be an important risk factor for hip fractures, which are associated with significant excess mortality, disability and economic costs. There is presently also disturbing evidence of rickets reappearing in Europe, particularly in immigrant populations. It has, in addition, been pointed out that the levels of parathyroid hormone seen in many Europeans, particularly in the winter, are high enough to indicate a degree of hyperparathyroidism, which could be associated, particularly in the rapidly growing young, with an undesirable departure from achievement of optimal bone mass.

Vitamin D fortification and/or supplementation strategies are an effective and reasonably cheap way of arresting preventable health consequences. But there are many unknowns in relation to the strategy of vitamin D fortification of food, particularly concerning the levels achieving optimal effects without toxicity.

### **OBJECTIVES**

The overall objective is to investigate whether fortification of food with vitamin D is a feasible strategy to remedy the insufficient vitamin D status of large population groups in Europe, and to determine at what level fortification should be pitched. The minimal effective dose with respect to vitamin D status, calcium metabolism and bone will be assessed in adolescent girls, elderly women and an immigrant population group. The seasonal variation of vitamin D status across Europe and the relative contributions of sun exposure and dietary habits, including food fortification and vitamin D supplementation will be evaluated in young and elderly. The technical feasibility of fortifying a low-fat food with vitamin D and the bio-availability of the incorporated vitamin will be determined, as well as the acceptability to the consumer.

### **(EXPECTED) RESULTS AND ACHIEVEMENTS**

This project aims -taking a long term view- at improving vitamin D status of the European population, and thus takes up many facets of general health with particular reference to bone integrity. The expected results should make it possible across Europe

- To tailor vitamin D fortification optimally with respect to population needs.
- To make use of a low-fat healthy food as fortification vehicle in accordance with European nutrition recommendations
- An important outcome is to reinforce the scientific base for recommendations on vitamin D as a nutrient.



**TOWARDS A STRATEGY FOR OPTIMAL  
VITAMIN D FORTIFICATION**



QLK1-2000-00623: Towards a strategy for optimal vitamin D fortification

**Coeliac disease: A food induced disorder.**  
**Exploration and exploitation of T cell stimulatory gluten peptides**  
**GLUTEN EPITOPES IN CD**

<b>Contract number:</b> QLK1-2000-00657	<b>Coordinator:</b>
<b>Contract type:</b> Shared Cost Project	Prof. Dr Ludvig Sollid
<b>Total cost:</b> € 1.092.072	University of Oslo
<b>EC contribution:</b> € 1.092.072	Institute of Immunology
<b>Starting date:</b> 1/01/2001	Rikshospitalet
<b>Duration:</b> 36 Months	0027 Oslo
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## **Coeliac disease: A food induced disorder. Exploration and exploitation of T cell stimulatory gluten peptides**

### **BACKGROUND**

Coeliac disease (CD) is caused by intolerance to gluten, a common food protein. The disease affects approximately one million Europeans. There is strong evidence that CD is the result of aberrant T cell responses to gluten peptides bound to the disease predisposing Human Leukocyte Antigen (HLA-DQ) molecules. T cell recognition of many of these peptides is dependant on them being enzymatically modified in a way that promotes their binding to HLA-DQ. These results provide a rationale for the development of CD. In this project, the relative importance of the identified peptides will be determined, an *in vivo* effect of these peptides will be demonstrated, the feasibility of therapeutic intervention will be investigated, and reliable and easy-to-handle test systems for the detection of toxic gluten peptides in food products will be developed.

### **OBJECTIVES**

1. Quantify and characterise the adult and paediatric T cell responses directed at the gluten peptides identified. HLA-DQ/peptide tetramer staining, ELI-spot assays and intracellular IFN gamma staining will be exploited to establish the overall frequency of gluten specific T cells in coeliac mucosa and to assess the importance of T cell recognition of deamidated vs. non-deamidated gluten epitopes. This will provide new insights into the mechanisms of disease pathology and offer invaluable data for the optimal design of an assay to detect 'toxic' components of gluten.
2. Formal evidence that the T cell epitopes are associated with the toxicity of gluten will be provided by conducting peptide feeding trials in human coeliac volunteers. It is possible that oral challenge with pre-deamidated peptides will re-route the peptides into the pathways that normally ensure tolerance to food antigens. Therefore, we will investigate what effect feeding deamidated gluten peptides has on peptide specific T cells. This, and other therapeutic strategies unethical to explore in human volunteers, will be investigated in a humanised transgenic mouse model of CD. This work will provide a foundation for initiating human clinical trials investigating new methods to treat CD.
3. Stable cell lines expressing transfected T cell receptors specific for the major gluten epitopes will be generated. These transfectants will form the basis of a test-kit that will detect the toxic components of wheat in food products. The specificity and sensitivity of these T cell reagents will then be compared with a panel of antibodies raised to the same peptide epitopes to see if ultimately an ELISA based system with a similar specificity can be developed.

### **(EXPECTED) RESULTS AND ACHIEVEMENTS**

A detailed description of the T cell response to wheat in CD will be provided, and the relative importance of the different gluten epitopes will be identified. An *in vivo* demonstration of the toxicity of these peptides will be provided. The specificity of T cell transfectants and monoclonal antibodies recognising the major gluten epitopes will be compared.

The knowledge and reagents from generated within this project will form the basis for a novel T cell based test-kit that will allow, for the first time, the direct detection of toxic gluten in food.

**Functional assessment of interactions  
between the human gut microbiota and the host  
EU AND MICROFUNCTION**

**Contract number:** QLK1-2001-00135  
**Contract type:** Shared Cost Project  
**Total cost:** € 2.238.374  
**EC contribution:** € 1.739.074  
**Starting date:** 1/01/2002  
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## **Functional assessment of interactions between the human gut microbiota and the host**

### **BACKGROUND**

The aim is to identify the effects of dietary modulation of the human gastrointestinal microflora. The influence of live microbial feed supplements (probiotics), dietary carbohydrates known to have a selective metabolism (prebiotics), and a combination of these two approaches (synbiotics) will be ascertained. The main objectives are to clarify effects on the normal gut microflora, and on host gastrointestinal function, as well as determine mechanisms involved in pro, pre and synbiotic functionality. These objectives will be achieved through exploitation of model systems and state-of-the-art technology. It is anticipated that a successful project will have much relevance for consumers, clinicians, nutritionists and microbiologists. In addition, the identification of host-microbe interactions will facilitate impetus into functional foods in the EU.

### **OBJECTIVES**

Principal objectives are to determine the efficacy and safety of probiotics and prebiotics, determine effective doses/combinations, identify mechanisms of action and investigate impacts on host function. An important aspect will be the development of new synbiotics and their use in a human trial.

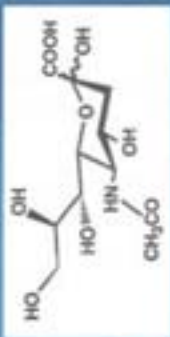
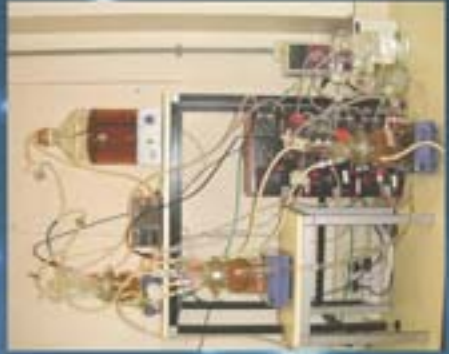
The work planned aims to identify the mechanisms of effect and to produce valuable information on the influence of dietary intervention on the activities of human gut microflora. In addition, it provides an essential means of validating probiotics and prebiotic, and will give information on the optimal combinational approach.

There is now an imperative requirement to identify the realistic health outcomes associated with probiotic and prebiotic intake and, importantly, give rigorous attention towards determining their mechanisms of effect. This project will aim to do so through investigating probiotic and prebiotic influence on host functionality - including microbiological and physiological aspects.

### **(EXPECTED) RESULTS AND ACHIEVEMENTS**

The aim is to identify mechanistic interrelationships through fundamental scientific approaches. Over four years, 35 scientific deliverables will have been met resulting in the milestones: efficient prebiotics and required dosage; active synbiotics; effects of functional foods on bacterial translocation; effects on host gene interactions; safety of functional foods determined; effects on selected health indices in humans.

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QLK1-2001-00135: Functional assessment of interactions between the human gut microbiota and the host

**Influence of dietary fatty acids on the pathophysiology of  
intrauterine foetal growth and neonatal development  
PERILIP**

**Contract number:** QLK1-2001-00138  
**Contract type:** Shared Cost Project  
**Total cost:** € 1.705.854  
**EC contribution:** € 1.705.854  
**Starting date:** 1/04/2002  
**Duration:** 36 Months  
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## **Influence of dietary fatty acids on the pathophysiology of intrauterine foetal growth and neonatal development**

### **BACKGROUND**

Perinatal nutrition is known to affect the health and development of the newborn child. A foetus that suffers intra-uterine growth restriction (IUGR) is more likely to suffer from cardiac or diabetic problems in later life, an effect known as “metabolic programming”. Particular fatty acids are required for development but the optimum composition of dietary lipids remains controversial. The project will compare normal and IUGR pregnancies in terms of maternal, neonatal and placental fatty acid profiles. Placental transfer of fatty acids *in vivo* and the functional ability of trophoblasts *in vitro* will be measured. The effects of dietary fats, on maternal endocrine status, oxidative stress, milk composition, placental function and on the development of IUGR and normal foetuses *in utero* (or *ex utero* in the case of the preterm infants fed intravenously) will be assessed. Studies in humans will be complemented with appropriate rat and pig animal-models. The results will be used to formulate improved dietary recommendations for mothers throughout pregnancy and lactation.

### **OBJECTIVES**

The overall objective of PERILIP is to define the role of fatty acids in foetal growth and neonatal development, with particular reference to intra-uterine growth restriction (IUGR). The ultimate goal is to improve dietary guidelines for human pregnancies. Specific objectives are:

- To determine the fatty acid profiles of foetuses with different patterns of intrauterine growth.
- To determine those factors which can influence the availability of specific fatty acids to the foetus and to the neonate (e.g. diet, the composition of maternal adipose tissue, maternal endocrine status, placental function and milk composition).
- To identify the consequences, for placental function, foetal growth, neonatal development and perinatal oxidative characteristics, of manipulating the dietary fatty acid composition.
- The production of specific dietary recommendations for pregnant and lactating women.

### **(EXPECTED) RESULTS AND ACHIEVEMENTS**

- The differences in fatty acid status of foetus, placenta and mother in IUGR and normal pregnancies
- The roles of diet, maternal fat stores, hormonal status and placental function in providing fatty acids to the foetus, and to the neonate via lactation
- The ways in which manipulation of diet can affect development, milk composition, placental function, hormonal status and oxidative stress.
- Dietary recommendations for maternal nutrition at different stages of pregnancy and lactation.



## PERI LIP

Improving the nutrition of the growing foetus and its mother



- Which dietary fats?
- How much?
- When?



QLK1-2001-00138: Influence of dietary fatty acids on the pathophysiology of intrauterine foetal growth and neonatal development

**Zinc effects on nutrient/nutrient interactions and trends in health  
and ageing  
ZENITH**

**Contract number:** QLK1-2001-00168  
**Contract type:** Shared Cost Project  
**Total cost:** € 2.786.141  
**EC contribution:** € 1.909.050  
**Starting date:** 1/03/2002  
**Duration:** 36 Months  
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## **Zinc effects on nutrient/nutrient interactions and trends in health and ageing**

### **BACKGROUND**

Intake of protective nutritional components, including zinc, is critical for older people. Zinc enrichment may be beneficial for health, but excess zinc may interact with Fe and Cu metabolism. We propose to determine the response to nutritional supplementation of zinc in cohorts of late middle-aged and older men and women from different European countries. Volunteers will receive a placebo or two levels of zinc supplement for 6 months. Effects of zinc supplementation on relevant micronutrient status and intestinal absorption of zinc will be evaluated. Cognitive function and psychological and physiological factors will be monitored. Beneficial effects and possible adverse effects, on surrogate biomarkers of health and physiological factors, will be determined at baseline, 3 and 6 months of zinc supplementation. This proposal will provide a scientific basis for formulation of public health recommendations on dietary zinc intake in ageing Europeans.

### **OBJECTIVES**

The overall aim is to provide clear and sound scientific data on the beneficial and/or potential adverse effects on mental and physical health of zinc supplementation in ageing Europeans in order to evaluate the need for dietary recommendations specific to this population.

The specific objectives are on the one hand an estimation of zinc intake and status in late middle-aged and older people in four European countries. On the other hand, the project is aimed at the determination of zinc supplementation effects on mood, taste, food choice, cognitive function, anti-oxidant status and oxidative damage, immune status, physical activity, basal metabolic rate and thyroid function, protein synthesis, bone health, micronutrient status, and lipid metabolism.

### **(EXPECTED) RESULTS AND ACHIEVEMENTS**

We expect to demonstrate that high intakes of dietary zinc are beneficial to psychological and physiological health without adverse effect for these population groups. The knowledge acquired in this project will provide a scientific basis to decide whether specific dietary recommendations for zinc are required for this population.

**The role of lipids in neurodegeneration and their preventive potential  
in diet  
LIPIDIET**

<b>Contract number:</b> QLK1-2001-00172	<b>Coordinator:</b>
<b>Contract type:</b> Shared Cost Project	Dr Tobias Hartmann
<b>Total cost:</b> € 2.888.035	University of Heidelberg
<b>EC contribution:</b> € 2.208.750	Zentrum für Molekulare Biologie
<b>Starting date:</b> 1/01/2002	Heidelberg
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## **The role of lipids in neurodegeneration and their preventive potential in diet**

### **BACKGROUND**

To prevent and treat age associated neurodegenerative diseases is a key challenge of this century. Based on recent findings it is promising to develop dietary lipid related disease prevention strategies. The present project will undertake this strategic approach which will first be applied to Alzheimer's disease, in which brain lipids are believed to play an important role. Three converging lines of investigation will be pursued. In vitro studies of the role of lipids in neuronal degeneration and of the effects thereon of distinct lipid related treatments will be preformed first. The resulting promising treatments will than be used for the preparation of formulations whose effectiveness will be tested in vivo utilising distinct models of neurodegeneration and dementia. The best diets will be tested in man for their ability to halt and prevent disease.

### **OBJECTIVES**

The objective of this proposal is to develop and evaluate lipid diets and related food additives for their preventive and treatment-related beneficial effects on age related brain neurodegeneration and Alzheimer disease (AD). This will be done by experiments directed at this complementary and interrelated lines of investigation:

- Cellular and molecular studies of the role of lipids in brain neurodegeneration and effects of distinct lipid related treatments on neuronal function;
- Formulation of promising lipid related treatments and assessment, utilising in vivo models of brain neurodegeneration and AD, of their bioavailability and effectiveness;
- Lipid diet studies in man, to slow down and eventually prevent disease. The chronic nature of neurodegeneration and bioavailability render this lipid diet approach particularly promising.

### **(EXPECTED) RESULTS AND ACHIEVEMENTS**

Lipid modulation of APP, A $\beta$  and PS processing. Epidemiological results on early cholesterol levels, dietary habits for later in life diseases, pharmacokinetics of 20 lipid treatments, electrophysiology, 5 diets for in vivo use with preventive potential, ApoE3 and ApoE4 effects, in vivo effects, safety, influence on peripheral lipid metabolism, neurological preventive diet, dietary advice.

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QLK1-2001-00172: The role of lipids in neurodegeneration and their preventive potential in diet

**Local Mediterranean food plants:  
Potential new nutraceuticals and current role in the Mediterranean diet  
LOCAL FOOD-NUTRACEUTICALS**

**Contract number:** QLK1-2001-00173  
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**Total cost:** € 1.733.920  
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**Starting date:** not yet determined  
**Duration:** 36 Months  
**Scientific Officer:** Antonio di Giulio  
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## **Local Mediterranean food plants: Potential new nutraceuticals and current role in the Mediterranean diet**

### **BACKGROUND**

The EU health food market requires new products that can be used as high quality health food supplements (HFS). Many rural areas, esp. in the Mediterranean, have locally used traditional foods with potential positive effects on health and on ageing-related pathologies that now are only known by elderly people. The Consortium intends to study this local knowledge ethnobotanically and contribute to the development of new HFS. We plan to evaluate >150 species of food plants in a variety of primary in vitro assays (incl. CRE for memory formation, PPAR mediated transcriptional activity for diabetes type II, a series of 4 cell-based antioxidant assays, inhibition of eicosanoid generation). Active samples will then be studied in mechanistic in vitro/in vivo models focusing on the CNS and the cardiovascular system (CVS), e.g. free radical generation, membrane fluidity, antioxidative enzymes (CNS); vasorelaxant NO, vascular endothelial function (CVS).

### **OBJECTIVES**

The Consortium will contribute to the development of new nutraceuticals and identify plant extracts traditionally used in rural communities of Southern Italy, Greece and Southern Spain as dietary by-products with potent anti-oxidant, anti-diabetes and memory mediating activity. Additionally, it will contribute to a fuller evaluation and development of the Mediterranean diet with a focus on local dietary plants (and fungi) and plant derived products.

### **(EXPECTED) RESULTS AND ACHIEVEMENTS**

- Ethnobotanical documentation of food products of selected communities in Southern Italy, Spain, Greece incl. Crete
- Comprehensive data on social, cultural, economical framework
- Identification of active extracts/pure compounds (leads for new HFS)
- Biochemical/pharmacological in vitro mechanisms/in vivo effects of selected species
- Dissemination of ethnobotanical information in local/national languages





QLK1-2001-00173: Local Mediterranean food plants: Potential new nutraceuticals and current role in the Mediterranean diet

## Alcohol related cancers and genetic susceptibility in Europe ARCAGE

**Contract number:** QLK1-2001-00182  
**Contract type:** Shared Cost Project  
**Total cost:** € 2.124.222  
**EC contribution:** € 2.085.727  
**Starting date:** 1/01/2002  
**Duration:** 42 Months  
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## Alcohol related cancers and genetic susceptibility in Europe

### BACKGROUND

Each year there are approximately 80,000 cases and 40,000 deaths of cancer of the upper aero-digestive tract (UADT) in the 15 EU countries, making it the fourth most common cancer in the EU. The proposed study will recruit over 2500 cases of UADT cancers and a group of comparable controls in 9 centres of the EU. It will test specific hypotheses including genetic susceptibility to alcohol metabolism, patterns of alcohol consumption and types of alcohol beverage, and dietary factors including low consumption of fruits and vegetables. Subsequently, it will investigate why some countries have incidence rates over 4 times greater than other countries. By incorporating information on genetic susceptibility, alcohol, dietary and other lifestyle patterns, the study will aim to identify individuals at a very high risk of developing UADT cancers.

### OBJECTIVES

The objectives will be to identify the reasons behind the wide differences in UADT cancers in Europe, including different genetic susceptibility to alcohol metabolism, different genetic susceptibility to tobacco metabolism and DNA damage, different patterns of alcohol consumption and types of alcoholic beverage, and interaction between high alcohol consumption and other agents including genetic factors, other dietary factors, and lifestyle factors.

### (EXPECTED) RESULTS AND ACHIEVEMENTS

The study will critically test the relationship between alcohol consumption, diet and genetic susceptibility to UADT cancers, and assess the extent to which these factors may be used for identifying individuals at high risk of developing the disease. A database of all dietary information will be established as well as a biological bank of blood and serum samples.

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## Dietary lipids as risk factors in development: Mechanistic issues DLARFID

**Contract number:** QLK1-2001-00183  
**Contract type:** Shared Cost Project  
**Total cost:** € 3.109.378  
**EC contribution:** € 2.529.092  
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## **Dietary lipids as risk factors in development: mechanistic issues**

### **BACKGROUND**

Beta-carotene, the source of the lipid soluble vitamin A and retinoic acid in humans was recommended for the prevention of atherosclerosis and cancer development. Unexpectedly, the recent three multicentre, randomised human trials revealed the weak protective effect against the increased incidence of myocardial infarction and morbidity/mortality due to the lung cancer. Since beta-carotene is commonly used as the food colorant, the influence of its metabolites together with fatty acids (FA) derivatives (known regulators of nuclear receptors) will be investigated in the healthy and cancer human and animal cells. The possible involvement of the new classes of proteins and genes (gene clusters) will be followed by the most modern methods to determine the early markers of pathology which would serve as the new diagnostic measure for the cancer hazard determination and understanding of the food and consumer safety.

### **OBJECTIVES**

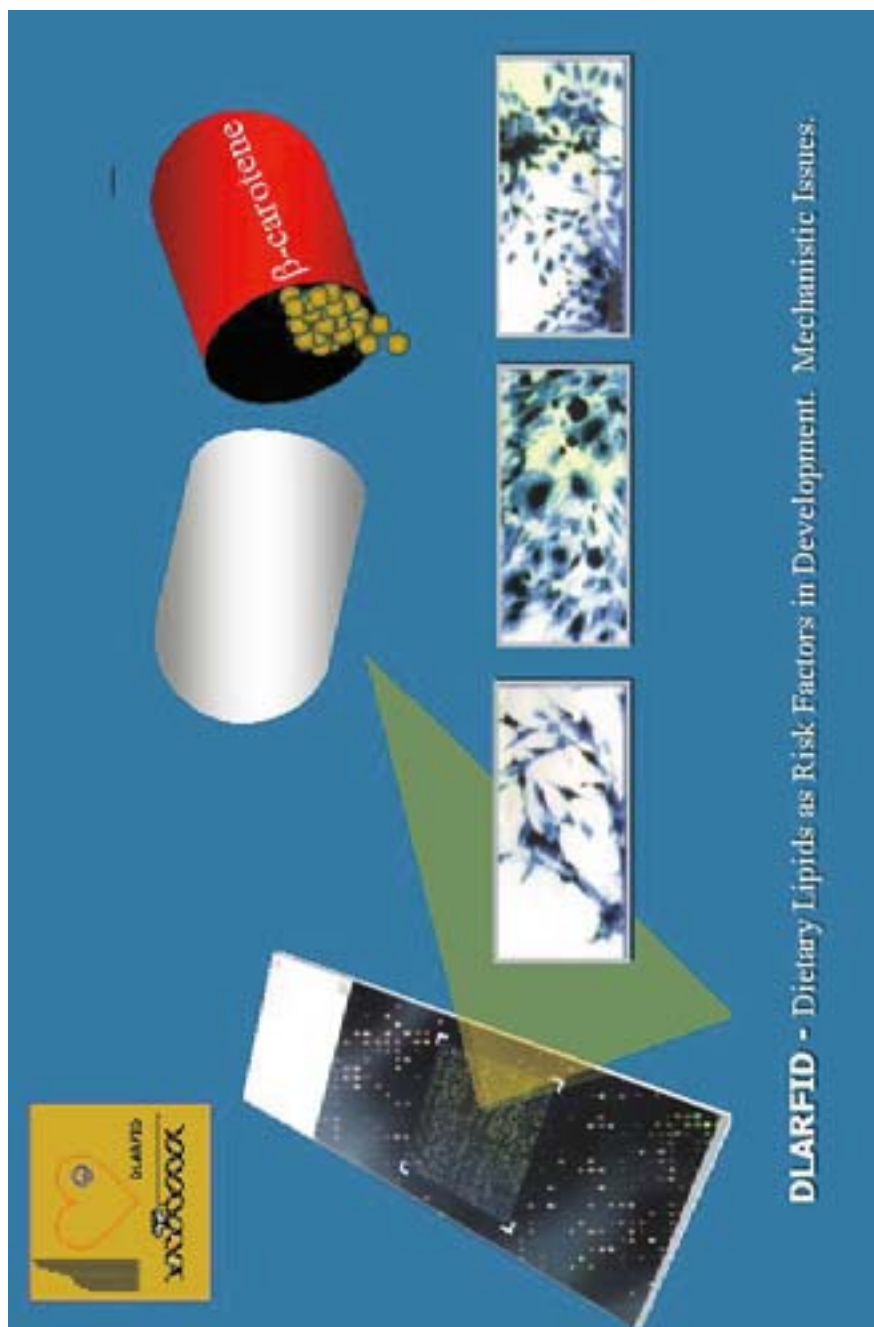
- To establish the hazard of consumer health, well-being and to enhance industrial competitiveness by eliminating the undesirable, health threatening effect of such component as the beta-carotene derivatives affecting together with fatty acids (food lipids) the growth and differentiation of mammalian cells.
- To develop the future prevention strategies against the hazard of food-induced cancer outgrowth at the high-risk states such as obesity (accumulation of fatty acids and lipid-soluble carotenoids in tissue) in humans.
- To allow the partners to use and exchange highly specialised technology for the benefit of research, the development of knowledge within the European community, reduction or elimination of the differences between pre-accession states such as Poland and EU members.
- The results will support the development of the dietary or pharmacological, gene expression modifying therapeutic strategies aiming to prevent illnesses connected with non-controlled cellular proliferation.

### **(EXPECTED) RESULTS AND ACHIEVEMENTS**

- Development of advanced molecular biology and proteomic methods for studying beta-carotene and FA responsive genes.
- Identification of FA and beta-carotene induced genes, gene products or processes that may play a role in beta-carotene and FA stimulated cell growth, differentiation and apoptosis (in vitro and in vivo).
- Determination of possible hazard or benefit (diagnostic and therapeutic implications) and preparation of statement concerning the safety of beta-carotene and FA food supplementation.

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QLK1-2001-00183: Dietary lipids as risk factors in development: Mechanistic issues

**Isoflavones for reducing risk of coronary heart disease  
among postmenopausal women  
ISOHEART**

**Contract number:** QLK1-2001-00221  
**Contract type:** Shared Cost Project  
**Total cost:** € 2.573.771  
**EC contribution:** € 2.263.046  
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## **Isoflavones for reducing risk of coronary heart disease among postmenopausal women**

### **BACKGROUND**

Prevalence and mortality of cardiovascular disease (CVD) increase in women after menopause. This has been attributed to the loss of the cardioprotective actions of oestrogen at menopause. Isoflavones are naturally occurring plant derived nonsteroidal oestrogen mimics. Animal and preliminary clinical evidence suggest that isoflavones could reduce risk of CVD. The objective of this project is to evaluate the potential health beneficial effects of soy isoflavone enhanced foods in a randomised controlled trial in postmenopausal women. A wide range of risk markers for CVD and new biomarkers for endothelial cell function will be measured. Genomic and proteomic techniques will be applied to identify biomarkers of physiological response. Consumer perspectives on isoflavone enhanced foods will be assessed.

### **OBJECTIVES**

- To establish a multidisciplinary scientific basis for nutritionally enhanced food products designed to promote women's health.
- To document the presumed health benefits of isoflavone enhanced foods consumed by older women as identified by positive changes of markers of cardiovascular disease risk.
- To identify new biomarkers of potential beneficial response to isoflavones.
- To provide benchmark results for soy isoflavones to be used for identifying alternative European produced sources of isoflavones.
- To provide quantitative, qualitative and comparative documentation of social, cultural and socio-psychological factors that impact upon consumer acceptability of isoflavone enhanced foods among postmenopausal European women.

### **(EXPECTED) RESULTS AND ACHIEVEMENTS**

Major milestones: selection of foods for intervention (mth 5); identification of biomarkers of endothelial cell function (mth 15); completion of intervention (mth 24); scientific papers and final reports (mth 36). The project will provide interdisciplinary scientific data for the potential cardioprotective role of soy isoflavones as well as for consumer perspectives on isoflavone enhanced foods. New biomarkers will be evaluated.





QLK1-2001-00221: Isoflavones for reducing risk of coronary heart disease among postmenopausal women

# The effect of olive oil consumption on oxidative damage in European populations

## EUROLIVE

**Contract number:** QLK1-2001-00287  
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## **The effect of olive oil consumption on oxidative damage in European populations**

### **BACKGROUND**

EUROLIVE is a European multi-centre clinical nutritional trial concerning the effect of a traditional Mediterranean antioxidant-rich food, olive oil, on oxidative stress and damage to lipids and DNA in humans. EUROLIVE also aims at studying the bioavailability and the binding of olive oil phenolics compounds to low-density lipoproteins. Our study will focus on whether a reasonable supplemental amount of refined (without phenolics), common (with low phenolic content) and extra virgin (with high phenolic content) olive oil would reduce lipid peroxidation and DNA oxidation in 180 humans from 3 European populations (Northern, Central and Southern), and whether there are differences on the effects according to the olive-oil phenolic concentration. The market prices of olive oil differs being refined and common olive oil cheaper than virgin olive oil.

### **OBJECTIVES**

- To compare the impact of olive oil, and antioxidant-rich foodstuff, on oxidative damage and low-density lipoprotein (LDL) fatty acid composition across selected European countries.
- To investigate the bioavailability of olive oil phenolic compounds in humans.
- To determinate the relation between olive oil ingestion and the binding of phenolic compounds to LDL.
- To explore differences among healthy men from different European areas in lipid peroxidation and fatty acid composition of LDL.
- To determine whether addition or substitution of monounsaturated fat results in better LDL fatty acid composition after three months of olive oil administration in Central and Northern European participants.

### **(EXPECTED) RESULTS AND ACHIEVEMENTS**

Milestones; consortium agreement signature and meetings; common protocol and instruments to determine basal variables (non-laboratory data). Olive oil analyses. Bioavailability and clinical trials complexation. Laboratory measurements complexation. Common edited data base. Scientific manuscripts. Dissemination manuscript for European consumers. We expect to observe differences in the impact of olive oil consumption on oxidative damage across European areas and to deliver accurate recommendations for olive oil consumption.

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QLK1-2001-00287: The effect of olive oil consumption on oxidative damage in European populations

**Consumer trust in food: A European study  
of the social and institutional conditions for the production of trust  
TRUSTINFOOD**

<b>Contract number:</b>	<b>QLK1-2001-00291</b>	<b>Coordinator:</b>	Dr Unni Kjærnes
<b>Contract type:</b>	Shared Cost Project		The National Institute for Consumer
<b>Total cost:</b>	€ 2.005.640		Research
<b>EC contribution:</b>	€ 1.678.960		PO Box 173
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## **Consumer trust in food: A European study of the social and institutional conditions for the production of trust**

### **BACKGROUND**

The President of the European Commission, Romano Prodi, gave considerable attention to questions of food safety in his speech to the Third Annual Assembly of Consumer Associations at the 23rd November 2000. He emphasised the importance of protecting the health of the citizens as well as "...the need to restore their confidence in the safety of food itself, in our food law and the institutions, organisations and structures developing the food law...". The present knowledge indicates that levels of consumer trust in food vary considerably across Europe. Some differences can be explained by the absence or presence of food scandals, but the seriousness of such scandals do not seem to be inversely correlated with consumers' trusting level. The levels of trust and distrust may also be influenced by institutional arrangements, dominant actors and varying responses to problematic events. Consequently, a multidisciplinary study is needed to identify and analyse the factors that determine trust in the food supply by means of comparative analyses including several types of data.

Taking actively into account the last food crises, it is clear that the studies are need in the following two cases: beef - a sector in crisis and transformation, and tomatoes - a less challenged sector.

### **OBJECTIVES**

The overall objective is to investigate the social and institutional conditions for the production and maintenance of consumer trust in food. The specific objectives are to:

- develop valid measures of consumer trust and distrust in food, its social and institutional determinants in a cross-country context ;
- describe dimensions and variations of trust among consumers in various countries and social groups;
- identify main characteristics of and recent changes in national food policy systems that may be associated with consumers' responses to food safety issues ;
- chart changes and identify strategies and institutional arrangements for the promotion of trust within EU institutions and key organisations at the European level;
- compare institutional conditions, identify concerns and priorities among strategic actors in the food system across 6 European countries at various levels (regional (when relevant), country, EU) and identify different trust regimes;
- explore and specify key institutional factors which affect consumer trust from the perspective of norms, decisions and routines;
- establish a dialogue with consumer representatives to a) discuss interpretations of relevant project findings and EU policy objectives and b) develop strategic proposals that can strengthen the position of consumers in decision-making processes.
- invite public authorities to workshops in order to discuss implementation of results and implications for trust enhancing strategies.
- bring out implications of research findings for relevant user groups.

## (EXPECTED) RESULTS AND ACHIEVEMENTS

- A multi-faceted, interdisciplinary analysis of the basis of consumer trust and distrust in food provision in contemporary Europe.
- A thorough comparative analysis of the effects of different institutional arrangements, country by country, which bear upon consumer trust/distrust in food.
- An analysis of the degree of convergence of institutional procedures in Europe as a consequence of EU policy initiatives.
- A policy-relevant appreciation of the role of citizens and consumer organisations in articulating the interests of consumers in the purpose of establishing a trustworthy European food system.
- A critical analysis of alternative strategies for handling trust and distrust in the food system.



QLK1-2001-00291: Consumer trust in food: A European study of the social and institutional conditions for the production of trust

## Nutritional primary prevention of type 1 diabetes DIABETES PREVENTION

**Contract number:** QLK1-2001-00372  
**Contract type:** Shared Cost Project  
**Total cost:** € 1.758.219  
**EC contribution:** € 1.653.470  
**Starting date:** 1/05/2002  
**Duration:** 48 Months  
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## Nutritional primary prevention of type 1 diabetes

### BACKGROUND

Type 1 diabetes in children is a major health problem in Europe, and the incidence of the disease is increasing. The consequences and costs of Type 1 diabetes presenting in childhood are immense. Type 1 diabetes develops in genetically susceptible individuals, if one or several environmental factors lead to autoimmune destruction of the pancreatic beta-cells. Cow milk proteins are one of the main candidates among the environmental factors. The objective of the present proposal is to determine whether denial of nutritional cow milk proteins for at least the first 6 months of life reduces the incidence of Type 1 diabetes in children at increased genetic risk of developing the disease and/or the appearance of diabetes associated antibodies by the age of 6 years. The proposal is based on a pilot study in man indicating that it may be possible to modify spontaneous beta-cell autoimmunity by dietary intervention.

### OBJECTIVES

The overall objective of the project is to determine whether weaning to a casein hydrolysate (Nutramigen TM) during at least the first 6 months of life reduces the incidence of Type 1 diabetes in genetically susceptible children. An important study question is, whether casein hydrolysate effects are due to the avoidance of complex weaning diets such as cow's milk based formula. This question will be addressed by correlating cow's milk immune responses with autoimmune markers and with diabetes.

Within the time frames of the present application, the trial will answer specific questions:

- Specific Aim I: Will the intervention reduce the frequency of autoimmune markers of beta-cell destruction during the first 6 years of life in subjects with increased genetic risk for Type I diabetes?
- Specific Aim II: Are there relationships between cow's milk antibodies, a measure of cow's milk exposure, and autoimmunity to islet antigens?

### (EXPECTED) RESULTS AND ACHIEVEMENTS

We will recruit and identify newborn infants with an increased genetic risk for Type 1 diabetes (Milestone 1), implement a dietary intervention in infancy (Milestone 2) to attempt to decrease the incidence of the disease (Milestone 3), and collect blood samples at follow-up visits to measure the effect of the intervention on the appearance of immunological markers of Type 1 diabetes (Milestone 4).

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QLK1-2001-00372: Nutritional primary prevention of type 1 diabetes

## Childhood obesity: Programming by infant nutrition? CHOPIN

**Contract number:** QLK1-2001-00389  
**Contract type:** Shared Cost Project  
**Total cost:** € 2.832.821  
**EC contribution:** € 2.422.807  
**Starting date:** 1/03/2002  
**Duration:** 42 Months  
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## **Childhood obesity: Programming by infant nutrition?**

### **BACKGROUND**

Obesity has become a global epidemic and represents a major health challenge all across Europe. Obesity poses serious short and long term health risks for the affected individual, as well as very high cost burdens for health care and social security systems. Development of effective prevention strategies which start in childhood are therefore desirable. In addition to genetic disposition and current lifestyle factors, early nutrient supply during infancy has a lasting, programming effect on later obesity risk. A high protein content in the diet during the first months of life, as is frequently experienced with current feeding concepts of formula and complementary foods, may predispose to an increased risk of later obesity. CHOPIN will investigate whether infant feeding regimes which differ in their protein and fat contents during the first two years of life influence an innovative, early marker of obesity development, namely the difference between length at two years of age and length at birth.

If a relationship between dietary protein and fat (or their ratio) and obesity risk is confirmed, effective obesity prevention by counselling of young families and development of modified infant food products is possible.

### **OBJECTIVES**

- To test the primary hypothesis that a possible causal factor for the difference in long-term obesity risk between breast and formula fed infants is the much lower protein content of breast milk compared to infant formulae.
- To do this by performing a double blind randomised multicentre intervention trial in healthy infants, comparing isocaloric infant formulae with high and low protein contents, balanced by fat.
- To validate the primary hypothesis with epidemiological observational studies evaluating the effects of different habitual protein intakes with traditional complementary feeding regimes in infants in the same 5 countries.
- To evaluate the relationship between different types of infant feeding regimes on a novel, early anthropometric marker or later obesity development, namely the difference between length at two years of age and length at birth.
- To investigate the effects of these infant feeding regimes on body composition, energy expenditure, physical activity, protein metabolism, renal function, leptin and its binding protein and on insulin like growth fact1 (IGF1).
- To disseminate the results widely to the user communities.
- to explore effective preventive strategies by modification of the composition and use of dietary products for infants and thus contribute to significant potential health benefits for the European population.

### **(EXPECTED) RESULTS AND ACHIEVEMENTS**

By 6m: Newsletter 1 and website established to report progress; methodologies agreed

15m-21m: Intervention study finished; Newsletter 2; Protocols published.

30m-36m: Observational study finished; Newsletter 3

By 36m: All analyses finished. Newsletter 4;

By 42m: Dissemination of results and conclusions from CHOPIN at major plenary conference; glossy brochures outlining achievements distributed widely to interest parties, Scientific Publications and Presentation.

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QLK1-2001-00389: Childhood obesity: Programming by infant nutrition?

**Stable isotope applications to monitor starch digestion and  
fermentation for the development of functional foods  
EUROSTARCH**

**Contract number:** QLK1-2001-00431  
**Contract type:** Shared Cost Project  
**Total cost:** € 1.782.370  
**EC contribution:** € 1.664.253  
**Starting date:** 1/01/2002  
**Duration:** 48 Months  
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## **Stable isotope applications to monitor starch digestion and fermentation for the development of functional foods**

### **BACKGROUND**

The aim of this project is to characterise the “metabolic quality” of carbohydrates, with the main focus on starch. With  $^{13}\text{C}$ -stable isotope techniques,  $^{13}\text{C}$ -glucose response to various  $^{13}\text{C}$ -starch sources will be studied, including functions that could modulate this response such as gastric emptying/intestinal transit time and digestion rates. These functions will be manipulated by addition of fat, protein, dietary fibre and enzyme inhibitors in order to optimise the glycaemic response. Fermentation of  $^{13}\text{C}$ -starch in man will be characterised by measuring small intestinal bioavailability,  $^{13}\text{C}$ -short chain fatty acid production and bacterial flora. This project will lead to a rationale for the development of breakfast food or biscuits with the target groups of healthy people, diabetic patients and people at risk to diabetes and obesity.

### **OBJECTIVES**

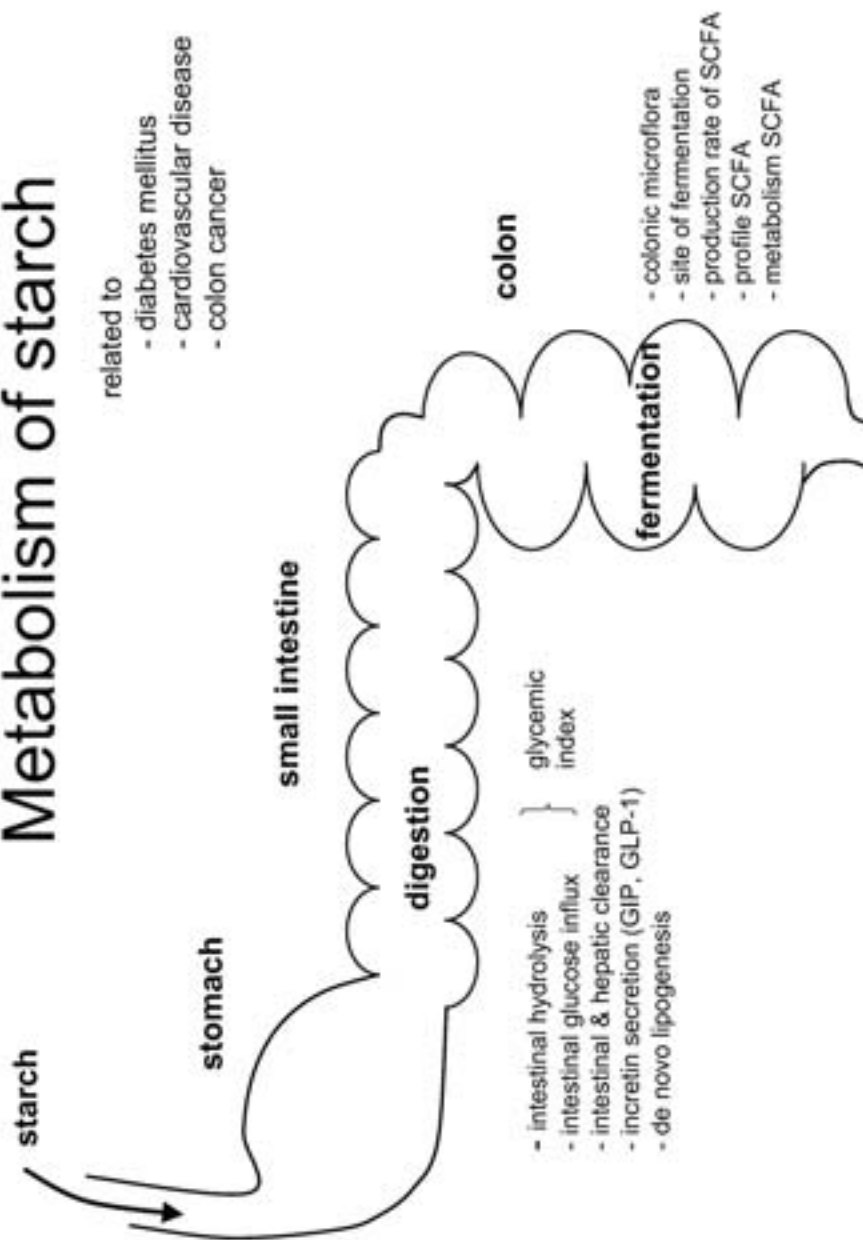
The European network SIGN (Stable Isotopes in Gastroenterology and Nutrition) aims to develop techniques and protocols using stable isotopes. These isotopes can be applied without any risk in human subjects for monitoring digestive and metabolic functions and evaluation of digestion of food.  $^{13}\text{C}$ -enriched substrates will be developed and incorporated in breakfast products or biscuits. Parameters influencing the glycaemic response of these substrates and products will be studied in vitro and by measuring the  $^{13}\text{C}$ -glucose response in serum. For studying carbohydrate fermentation, new stable isotope techniques and new techniques for analysis of microflora will be developed and applied. The specific starch containing products will be evaluated in healthy volunteers and diabetic patients.

### **(EXPECTED) RESULTS AND ACHIEVEMENTS**

- Availability of  $^{13}\text{C}$ -labeled starch and food products;
- Techniques for measuring starch digestion and fermentation;
- Assessment of the “metabolic quality” of  $^{13}\text{C}$ -starch containing products in healthy volunteers and diabetic patients;
- Health parameters related to industrial starch processing;
- Scientific basis for recommendations for the development of starch based functional foods;
- Definition of the role of the “glycaemic index” concept in communication strategies concerning healthy starch products.



# Metabolism of starch



QLK1-2001-00431: Stable isotope applications to monitor starch digestion and fermentation for the development of functional foods

## Iron in hemochromatosis: Deleterious effects of an essential nutrient NUTRIENT IRON TOXICITY

**Contract number:** QLK1-2001-00444  
**Contract type:** Shared Cost Project  
**Total cost:** € 2.624.534  
**EC contribution:** € 2.326.751  
**Starting date:** 1/05/2002  
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## **Iron in hemochromatosis: deleterious effects of an essential nutrient**

### **BACKGROUND**

Normal dietary iron causes organ damage in patients with homozygous Hereditary Hemochromatosis (HH). Heterozygotes (10% of the European population) are at risk for early cardiovascular death. HH patients absorb too much iron and have toxic non-transferrin-bound iron (NTBI) in plasma. This project intends to identify the mechanism of TBI toxicity, and the damage to vascular endothelium (as target for atherosclerosis) and to the liver. An inexpensive method for NTBI measurement will be developed. Oral iron chelators will be developed to inhibit excess absorption of iron and to scavenge NTBI. Iron absorption, as a key pathogenic mechanism, will be analysed at a molecular level. The project is expected to result in less organ damage and in prevention of early death in HH patients.

### **OBJECTIVES**

Iron is an essential nutrient, and its deficiency is worldwide an important cause of anaemia. Food and multivitamin fortification with iron is widely practised. This can have a deleterious effect in patients with hereditary hemochromatosis (HH), a frequent genetic disorder among Europeans. Normal amounts of dietary iron can lead to liver cirrhosis, diabetes, chronic arthritis, cardiomyopathy and liver cancer. Also heterozygotes (10% of all Europeans) are at risk, in particular for early cardio/cerebrovascular death. It is the objective to identify the mechanism of organ and vascular endothelium directed iron toxicity, to develop methods to measure toxic forms of iron in serum, to prevent these deleterious effects by identifying aggravating risk factors and designing iron chelators as safe food additives to scavenge toxic forms of iron.

### **(EXPECTED) RESULTS AND ACHIEVEMENTS**

The results will entail elucidation of:

- dietary, environmental and iron-related genetic risk factors for atherosclerosis and liver damage;
- a rapid, inexpensive method for measurement of toxic iron;
- design of oral iron chelators for prevention of iron damage;
- mechanisms of iron toxicity on liver, heart and endothelium;
- molecular mechanism of iron absorption in HH;
- offer advice to industry and nutritionists for prevention of iron damage in the population at risk.





QLK1-2001-00444: Iron in hemochromatosis: Deleterious effects of an essential nutrient

**Promoting and sustaining health through increased vegetable and fruit consumption among European schoolchildren**  
**PRO CHILDREN**

**Contract number:** QLK1-2001-00547  
**Contract type:** Shared Cost Project  
**Total cost:** € 1.337.251  
**EC contribution:** € 1.337.251  
**Starting date:** 1/04/2002  
**Duration:** 48 Months  
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## **Promoting and sustaining health through increased vegetable and fruit consumption among European schoolchildren**

### **BACKGROUND**

Fruits and vegetables (F&V) contribute to the prevention of chronic diseases. The current intake is below recommended levels in most European countries. The aim of this project is to identify determinants of F&V intake among school children, and to develop effective strategies to promote adequate consumption levels. Cross-sectional surveys will be implemented in representative samples of school children in nine European countries, and a comprehensive intervention programme will be developed and tested in three countries. It is expected that the project will provide important insight into F&V consumption patterns in different countries and into psychological and socio-demographic determinants of such consumption patterns. The project is also expected to result in a set of intervention strategies appropriate and effective in promoting F&V among school children and their parents across Europe.

### **OBJECTIVES**

- To develop valid and reliable instruments for assessing fruits and vegetables consumption and factors influencing the consumption patterns among school children and parents;
- To determine the consumption levels of fruits and vegetables and factors influencing the consumption of fruits and vegetables among school children and their parents in participating countries and in various sub-groups (such as gender, socio-economic groups and cultural background) and across countries.
- To design culturally relevant, but theoretically similar intervention programmes to be implemented in three participating countries. These programmes will all include a school-based education and food service component, as well as family involvement.
- To determine the applicability, impact, effect and cost-effectiveness of the intervention.

### **(EXPECTED) RESULTS AND ACHIEVEMENTS**

The cross-sectional surveys among school children in nine countries assessing F&V consumption and its determinants will enhance our understanding of consumer choices and attitudes regarding F&V. The intervention programme in three countries will lead to a set of appropriate intervention strategies that are effective in promoting F&V among school children and their parents across Europe.

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QLK1-2001-00547: Promoting and sustaining health through increased vegetable and fruit consumption among European schoolchildren

# Food risk communication and consumers' trust in the food supply chain

## TRUST

**Contract number:** QLRT-2001-02343  
**Contract type:** Shared Cost Project  
**Total cost:** Under negotiation  
**EC contribution:** Under negotiation  
**Starting date:** not yet determined  
**Duration:** 36 Months  
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## **Food risk communication and consumers' trust in the food supply chain**

### **BACKGROUND**

The research investigates the antecedents of trust in information sources and risk management along the food chain and the mechanisms that determine the social diffusion of trust. It focuses on the evaluation strategies brought about by consumers to assess the reliability of the message, the way they process risk information with regards to different food hazards, and the cultural gaps between professional risk managers and laypeople. It examines the interplay of the various psychological, sociological, demographic, and economic factors at individual, market, and social level. The proposal aims at providing a better understanding of consumer demands, attitudes and perceptions, with special reference to trust and risk perception in the food chain, and developing better strategies to communicate more effectively to consumers issues surrounding food risk.

### **OBJECTIVES**

- To contribute to a more in depth understanding of the nature, determinants and processes of social diffusion of trust in food risk information and food risk management, namely regarding BSE and GMOs;
- To evaluate the strategies brought about by consumers to assess the reliability of the message, the way they process risk information with regards to different food hazards, and the cultural gaps between professional risk managers and laymen;
- To assess the economic impacts of different risk communication strategies in the food chain;
- To discuss and communicate research findings with policy makers, risk managers, consumers' organisations, and representatives of farmers and food industries at national and European level, concerning ways to promote more effective and ethically appropriate mechanisms for managing risk information about food related hazards.

### **(EXPECTED) RESULTS AND ACHIEVEMENTS**

Anticipated deliverables of this research project are

- new methods of understanding and assessing consumer trust and risk perceptions in the food chain;
- new concepts for more effective communication with the consumer, and for reinforcing consumer confidence in the safety of the food supply;
- creation of more transparent consensus platforms through the direct involvement of stakeholders
- models of consumer's choice which could eventually facilitate innovation of products.

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## Consumer decision-making on organic products CONDOR

**Contract number:** QLRT-2001-02446  
**Contract type:** Shared Cost Project  
**Total cost:** Under negotiation  
**EC contribution:** Under negotiation  
**Starting date:** not yet determined  
**Duration:** 36 Months  
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## **Consumer decision-making on organic products**

### **BACKGROUND**

The market for organically produced foods remains relatively small. If it is to increase then there needs to be a systematic and scientific examination of the consumer decision-making processes involved in the choice between organic and non-organic foods. This project brings together a multidisciplinary team to examine this topic. It combines the development of methods for the segmentation of consumers based upon values and the elicitation of affective (emotional) associations and moral concerns. It involves the development of a theoretically based consumer decision-making model and the testing of this model in several EU member states and in identified consumer segments. It will provide information on the role played by values and by affective associations and moral concerns in consumer decision-making on organic foods and provide novel insights into the marketing of organic foods in the future.

### **OBJECTIVES**

The overall objectives of CONDOR are:

- To provide a basic understanding of the processes involved in consumer decision-making on the purchase and consumption of processed and fresh organic foods;
- To model consumer choice of organic foods based on attitudes, values, affective and moral concerns over eight EU member states.

In order to achieve this, the project also has the following specific objectives:

- To develop methods for the elicitation of moral concerns and of emotional influences on the choice of organic foods;
- To develop methods for identifying segments of consumers based upon their values;
- To integrate these values, moral concerns and emotional components into an integrated model of consumer choice of organic foods;
- To test this integrated model of choice across EU countries and identified consumer segments.

### **(EXPECTED) RESULTS AND ACHIEVEMENTS**

CONDOR will provide:

- Novel methods for uncovering emotional and moral concerns which might influence the choice of organic foods;
- Methods for segmenting consumers based on their values;
- Databases of consumer attitudes, values, emotional and moral concerns in relation to organic foods;
- An understanding of cross-European differences in the impact of emotional and moral influences on the choice of organic foods;
- Dissemination to stakeholders, including industry, consumer groups and NGOs, via a website and through brochures and workshops targeted at particular stakeholder groups;
- A final report synthesising the implications for the European marketing of organic foods.

This project will be the first to examine attitudes and behaviour in relation to both fresh and processed organic foods and to do so across EU member states. It will provide a better understanding of the motivations underlying consumer behaviour and hence have direct implications for the development of EU industry in this area, for consumer representatives and for consumers themselves.

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**Choosing foods, eating meals: Sustaining independence and quality  
of life in older people  
SENIOR FOOD-QOL**

**Contract number:** QLRT-2001-02447  
**Contract type:** Shared Cost Project  
**Total cost:** Under negotiation  
**EC contribution:** Under negotiation  
**Starting date:** not yet determined  
**Duration:** 36 Months  
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## **Choosing foods, eating meals: Sustaining independence and quality of life in older people**

### **BACKGROUND**

The project will develop an integrated strategy to improve the nutritional well-being of older people and hence their independence and quality of life. It will identify the problems older people encounter in obtaining and preparing foods to meet their specific needs and preferences. Each stage in the process from purchase to consumption will be examined including food retail access, choice of products and meal preparation issues. The attitudes and beliefs that influence food choices will be surveyed including perceptions of food-related health risks, functional foods, nutritional claims and retail practices. The importance of activities related to food procurement will be reviewed including social roles and relationships, economic factors, health status and how these influence the quality of the diet. The project will lead to more effective systems of food delivery, product development and inform policy aimed at healthy ageing.

### **OBJECTIVES**

The key objectives are to generate longitudinal, qualitative and quantitative data on the relationship between food intake, nutrition, health and quality of life; to understand the specific food procurement and consumption requirements of older people living alone compared to those living with others; and to maximise implementation of the findings through active dissemination and consultation with stakeholders. The specific scientific objectives are to investigate: the extent to which convenience and health drive food selection; the interaction between food procurement and meal preparation skills; user satisfaction with food-related services; the role of formal and informal networks in food provisioning and consumption among older people; the role of meals in later life; and the relationship between food, nutrition, health and quality of life in older people.

### **(EXPECTED) RESULTS AND ACHIEVEMENTS**

Pan European-databases on food selection, food procurement & meal planning/preparation in later life (month 18); food-related services available to seniors, the role of formal & informal networks in food procurement & the role of meals in later life (month 24); the relationship between food, nutritional well-being, health and quality of life (month 34) Month 36: Final report, recommendations and workshops on optimising the role food in sustaining independence and quality of life in old age.

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**Improving health through dietary phytoestrogens: A pan-European network on consumers' issues and opportunities for producers**  
**PHYTOHEALTH**

**Contract number:** QLRT-2001-02453  
**Contract type:** Thematic Network  
**Total cost:** Under negotiation  
**EC contribution:** Under negotiation  
**Starting date:** not yet determined  
**Duration:** 36 Months  
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## **Improving health through dietary phytoestrogens: A pan-European network on consumers' issues and opportunities for producers**

### **BACKGROUND**

Given the potential benefits that phytoestrogen (PE) intakes in the range of 60...100 mg/d may have on cardiovascular risk, cancer risk and osteoporosis prevention, new means of increasing PE consumption in Europe are being explored. This proposal will lead to the establishment of a pan-European network of institutions dealing with safety and health effects of phytoestrogens, identification of optimal sources and processing technologies, building around a cluster of three EU funded RTD projects. The project envisages the organisation of scientific meetings, preparation of consensus papers, fact sheet for regulators, producers and consumers, on-line communication with all stakeholders, i.e. scientists, product manufacturers, consumers targeted to receive products, and regulatory authorities guaranteeing that benefits will overcome risks will be represented.

### **OBJECTIVES**

The proposal aims at coordinating research funded by the EU and by member governments in the area of phytoestrogens. A first specific objective is to find consensus about the health and safety of phytoestrogens, establish the acceptance by consumers and to review regulation of PE-enriched food products and supplements in Europe. A second specific objective is to review active compounds, existing sources, manufacturing techniques. A third specific objective is to communicate to opinion leaders and regulating agencies about health and safety of phytoestrogen preparations. A fourth specific objective is to highlight controversial areas and to give recommendations for research.

### **(EXPECTED) RESULTS AND ACHIEVEMENTS**

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**Effect of diet and lifestyle on risk of gastrointestinal infection and allergy in early life: Consumer knowledge, attitudes and needs**  
**INFABIO**

**Contract number:** QLRT-2001-02606  
**Contract type:** Shared Cost Project  
**Total cost:** Under negotiation  
**EC contribution:** Under negotiation  
**Starting date:** not yet determined  
**Duration:** 36 Months  
**Scientific Officer:** Barend Verachtert  
**Project website:** not yet available

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## Effect of diet and lifestyle on risk of gastrointestinal infection and allergy in early life: Consumer knowledge, attitudes and needs

### BACKGROUND

Although there is strong evidence for links between diet, lifestyle and gut microflora in infectious disease and allergy, there is little knowledge of the mechanisms and no established markers of risk to target treatment and advice for those infants at high risk. In this project, a multi-disciplinary team will investigate these problems across five countries in Europe with very different diet and lifestyle and different risks of allergy and childhood infection. New tools for establishing consumer attitudes to foods and feeding behaviour and to the relationship between lifestyle, diet and disease in infancy will be developed and applied in groups of infants in five countries in Northern and Southern Europe, participating in a either a cross sectional, allergy case control, or an intervention study of infant functional foods. The infants will provide faecal samples throughout the first year, and these will be used to identify risk factors and biomarkers for disease incidence. Data will be used for a variety of dissemination to health professionals, the food industry and consumers.

### OBJECTIVES

- Develop and apply new tools to analyse consumer needs and attitudes to food products, processes and labelling and to determine diet, feeding patterns and lifestyle including incidence of allergy, infection and illness during infancy in 5 European centres;
- Carry out sensory studies on food preferences of infants;
- Evaluate the influence of diet, feeding behaviour and lifestyle on biomarkers and risk factors and actual incidence of allergy, infection and illness in infants in Northern and Southern Europe;
- Identify risk factors for allergy and infection in infant faecal material in the first year;
- Evaluate changes in biomarkers and risk factors for allergy and infection in faeces of infants fed with a probiotic-supplemented (*Bifidobacteria bifidum*, *Bifidobacterium longum*) infant formula compared with a standard formula and in faeces of infants fed with a prebiotic-supplemented infant formula compared with a standard infant formula.

### (EXPECTED) RESULTS AND ACHIEVEMENTS

- New tools for measuring consumer attitudes and needs in Europe about infant products and nutritional guidelines;
- Data to inform nutritional guidelines and development of infant functional foods;
- Biomarkers and risk factors for allergy and gut infections in infancy;
- Database of food intake and illness in the first year of life in 5 countries;
- Data of effects of infant functional foods on biomarkers and risk factors for allergy and gastrointestinal infections.

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## The food, GI-tract functionality and human health cluster PROEUHEALTH

<b>Contract number:</b>		<b>Coordinator:</b>	Prof. Dr Tiina Mattila-Sandholm
<b>Contract type:</b>	Cluster		VTT Biotechnology
<b>Total cost:</b>	€ 16.992.298		P.O. Box 1500
<b>EC contribution:</b>	€ 12.404.334		02044 VTT
<b>Starting date:</b>	1/02/2001		Finland
<b>Duration:</b>	End: 31/12/2005		Tel.: +358-9-456 5200
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### CLUSTER PROJECTS

<b>QLK1-2001-00067</b> <b>CROWNALIFE</b> Functional food, gut microflora and healthy ageing Prof. Dr Joël Doré INRA Jouy-en-Josas, F	<b>QLK1-2001-00563</b> <b>PROGID</b> Probiotics and gastrointestinal disorders: Controlled trials of European Union patients Prof. Dr Fergus Shanahan University College Cork, IRL
<b>QLK1-2000-00108</b> <b>MICROBIAL DIAGNOSTICS</b> Development and application of high throughput molecular methods for studying the human gut microbiota in relation to diet and health Prof. Dr Michael Blaut Deutsches Institut für Ernährungsforschung Potsdam-Rehbrücke, D	<b>QLK1-2001-01179</b> <b>PROPATH</b> Molecular analysis and mechanistic elucidation of the functionality of probiotics and prebiotics in the inhibition of pathogenic microorganisms to combat gastrointestinal disorders and to improve human health Prof. Dr Luc de Vuyst Vrije Universiteit Brussel, B
<b>QLK1-2001-00135</b> <b>EU AND MICROFUNCTION</b> Functional assessment of interactions between the human gut microbiota and the host Prof. Dr Glenn Gibson University of Reading, UK	<b>QLK1-2001-01273</b> <b>PROSAFE</b> Biosafety evaluation of probiotic lactic acid bacteria used for human consumption Prof. Dr Herman Goossens Universiteit Antwerpen, B
<b>QLK1-2001-00146</b> <b>DEPROHEALTH</b> Probiotic strains with designed health properties Prof. Dr Annick Mercenier Institut Pasteur de Lille, F	<b>QLK1-2000-30042</b> <b>PROTECH</b> Nutritional enhancement of probiotics and prebiotics: Technology aspects on microbial viability, stability, functionality and on prebiotic function Prof. Dr Dietrich Knorr Technische Universität Berlin, D

## The food, GI-tract functionality and human health cluster

### BACKGROUND

This project brings together 64 research partners from 16 European countries in the quest to obtain greater knowledge of the role of the intestinal microbiota in human health and disease and to develop new functional foods and therapies. Eight complementary multicentre European projects are included in the cluster. They cover all aspects in the development of new probiotic foods, from designing molecular tools to study the ecology of the intestinal microbiota, to understanding mechanisms of bacterium-host interactions, providing solutions to food technology issues, and finally to conducting human clinical trials to assess efficacy in preventing or treating disease. For more details, please see the description of the projects elsewhere in this catalogue.

### OBJECTIVES

The cluster aims to provide:

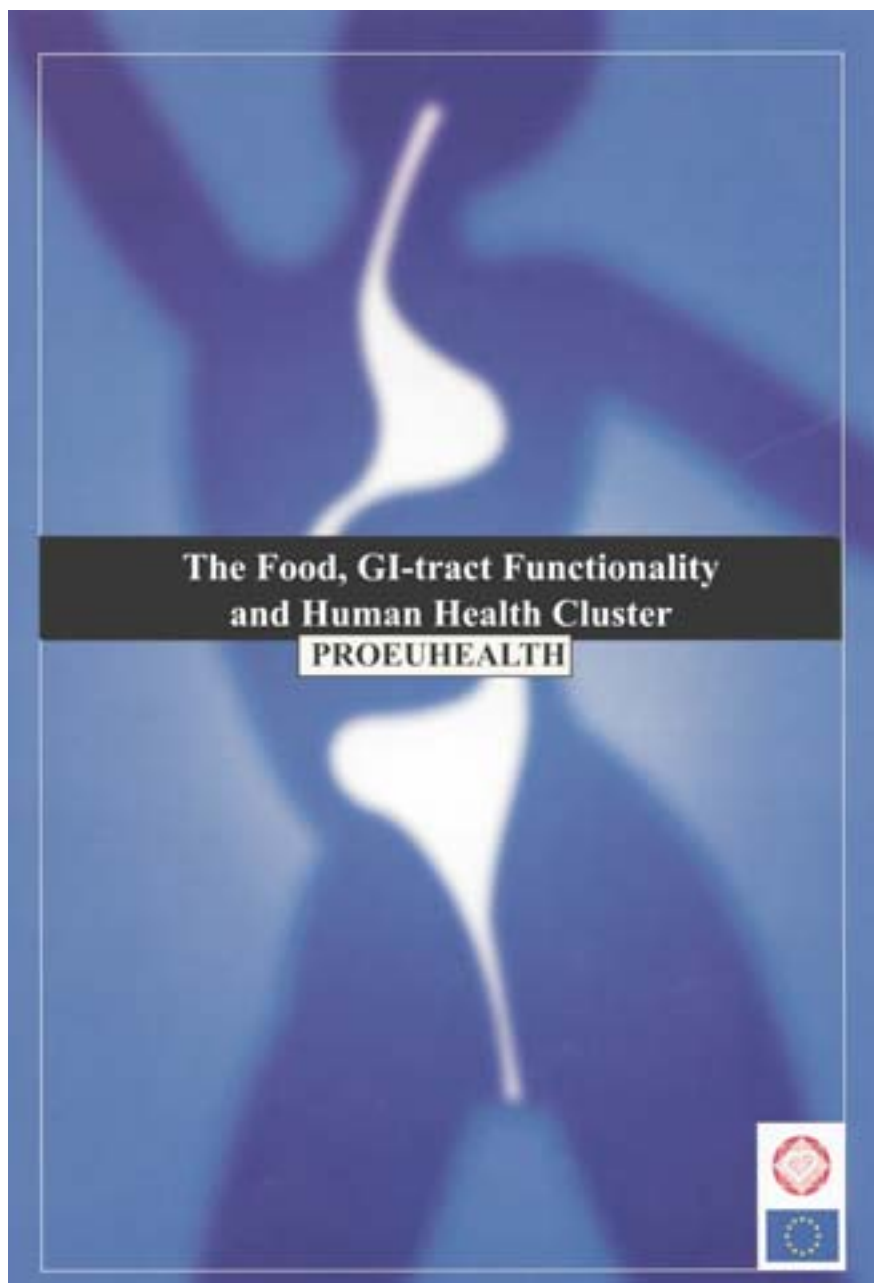
- A clearer understanding of the relationships between food, intestinal bacteria and human health and disease;
- New molecular research tools for studying the composition and activity of the intestinal microbiota;
- New therapeutic and prophylactic treatments for intestinal infections, chronic intestinal diseases, and for healthy ageing;
- A molecular understanding of immune modulation by probiotic bacteria and testing of probiotics as vaccine delivery vehicles;
- Biosafety evaluation of probiotics for human consumption
- Commercial opportunities for food and pharmaceutical industries.

### (EXPECTED) RESULTS AND ACHIEVEMENTS

The research innovations produced by the cluster will be disseminated to target audiences through three platforms:

- The Science Platform will provide an internal dissemination and networking platform for the cluster. The coordinator is Prof. Dr Willem de Vos, Agricultural University Wageningen (NL), email: willem.devos@algemeen.micr.wau.nl.
- The Industry Platform will enable the cluster to disseminate its research innovations to probiotic industries throughout Europe and the world and maximise the potential for commercial exploitation of results from the cluster's research. The coordinator is Prof. Dr Charles Daly, University College Cork (IRL), email: nfbcc@ucc.ie)
- The Consumer Platform will provide information to consumers about the cluster and its innovations in an appropriately tailored format, ensuring that the general public is kept informed and benefit from the research. The coordinator is Dr Liisa Lähteenmäki, VTT (FIN), email: liisa.lahteenmaki@vtt.fi.





The food, GI-tract functionality and human health cluster

**The infant nutrition cluster**  
**INFANT-NUTRITION-CLUSTER**

<b>Contract number:</b>		<b>Coordinator:</b>
<b>Contract type:</b>	Cluster	Dr Peter Dodds
<b>Total cost:</b>	€ 6.296.894	Imperial College at Wye
<b>EC contribution:</b>	€ 5.782.131	Department of Agricultural Sciences
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**CLUSTER PROJECTS**

QLK1-2001-00138

PERILIP

Influence of dietary fatty acids on the pathophysiology of intrauterine foetal growth and neonatal development

Dr Peter Dodds

Imperial College at Wye, UK

QLK1-2001-00372

DIABETES PREVENTION

Nutritional primary prevention of type 1 diabetes

Prof. Dr Hans Aakerblom

University of Helsinki, FIN

QLK1-2001-00389

CHOPIN

Childhood obesity: programming by infant nutrition?

Prof. Dr Berthold Koletzko

University of Munich, D




## FLAIR FLOW DEBATES

*The Flair-Flow National Network leaders organise each year in their country a debate in which invite scientists to respond to the questions asked by the end-users on a specific topic. These debates improve communication between the end-users and the scientific community.*

Examples of debates:

- Food quality - control and safety (AUSTRIA)
- Update on White Book on Food Safety (BELGIUM)
- Role of fats and oils in human nutrition (CZECH REPUBLIC)
- Organic foods (DENMARK & ITALY)
- Functional foods (FINLAND)
- Traditional food products and food safety (GREECE)
- Probiotics and Gut Health (HUNGARY)
- Safety of red meat (IRELAND)
- GMOs (POLAND & ROMANIA)
- Fat consumption and health status of population (SLOVAK REPUBLIC)
- Food irradiation (SPAIN)
- How to make best use of technology, and how to meet legislation requirements ? (UNITED KINGDOM)



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OPENS A DIALOGUE BETWEEN  
FOOD SCIENTISTS AND THE  
NON-SPECIALISTS, LIKE YOU!

**to know us better,  
go to the Project  
Information area.**

THE PROJECT MEMBERS' AREA  
IS NOT ACCESSIBLE TO THE PUBLIC.



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