MICROBES AND MAN
(MICMAN)

PROGRAMME MEMORANDUM

1 FOREWORD

The initiative to establish the Microbes and Man Research Programme has come from researchers working in the fields of medicine, nutrition research and environmental research in Finland. In response to this initiative, the Academy of Finland hosted an exploratory workshop on the subject of *Microbes and Man: Health, Nutrition and the Environment* at Gustavelund, Tuusula, on August 20-21, 2001. During the workshop several relevant research needs were identified, and this information was used as a basis for the preparation of the Microbes and Man Research Programme.

The Microbes and Man Research Programme will be jointly funded and implemented by several funding agencies including both national and international funding bodies. For the first time, funding collaboration has been established between the Academy of Finland and the Swedish Foundation for Strategic Research. The objective of international collaboration is to promote networking and training of researchers, to create and support enabling research environments and to increase scientific quality and international visibility of this research in both countries. The national partners in the implementation of the Microbes and Man Research Programme are the National Technology Agency and the Finnish Work Environment Fund. Co-funded research cooperation is in accordance with the European Research Area initiative of the European Union.

Microbes and Man will be a three-year programme running from 2003 through to 2005. The Programme invites applications from individual research teams and from consortia of several teams. Multidisciplinary and international cooperation is encouraged. The research projects which receive funding through the Microbes and Man Research Programme, are expected to work in close cooperation with one another, and to contribute to networking and training of researchers both nationally and internationally. The dissemination of research results in order to increase the impact of the programme is considered very important.

2 BACKGROUND

Microbes at the time of their discovery were primarily seen as agents causing disease, and indeed revolutionized the concept of infectious diseases. Their ubiquitous presence and beneficial effects both in our environment and as permanent colonizers of the surfaces of the human body have been known for 50 years. While important advances have been made in understanding, diagnosing, treating and preventing a variety of infectious diseases, the genetic potential for variability and adaptation of the microbes will very likely continue to produce new diseases and other challenges to research. One needs only to remember that diseases caused by HI virus, *Legionella*, *Helicobacter* or *Chlamydia pneumoniae* have been known for a few decades only.

At the same time, much less research has been devoted to understanding and utilizing the behaviour and effects of the quantitatively much larger body of microbes that live in peaceful coexistence with man and with our environment. The synergistic health effects of nutrition and intestinal microbes remain largely unexplored. Man’s own behaviour has brought about a wide range of changes in the environmental microflora that feed back upon our wellbeing.

One reason for the relative negligence of the resident and environmental microflora has been technical: many of these organisms have been difficult or impossible to handle with the

methods primarily developed for the cultivation and study of the agents of infectious diseases. Research on both beneficial and harmful interactions of the microbes with man has been encumbered by lack of appropriate technology and knowledge on the side of the host.

Recently developed technologies with rapidly increasing ranges of application have completely transformed microbiological research and the rest of the field of the biosciences. These include DNA microarrays, proteomics, bioinformatics, the development of biological models, visualization and imaging. Results from the human genome sequencing project (HUGO), and the genomic sequencing of many bacterial and viral species are new sources of valuable information. New microbes in the human microflora are continuously being discovered. The area of functional genomics and microarray technology contain powerful tools that open up possibilities to create molecular maps of host-pathogen interactions. Novel high-throughput technologies should now be used to study the intestinal microbial communities and the relations between this microflora and the development of the innate immunity. Research within these fields may also lead to the finding of new methods for diagnosis and intervention. The accumulated mass of information generated within these research fields adds to the demands on bioinformatics and other information techniques, which must be considered an indispensable part of research in this area today.

The need for intensified microbiological research has been recognized for a number of years in Finland. In 1996, based on an extensive evaluation of molecular biology and biotechnology research in Finland, the European Molecular Biology Organization (EMBO) recommended that steps be taken to address certain deficits in these fields. Basic research on human microflora has been discussed to be set out as a priority area for research within the EU.

3 OBJECTIVES OF THE PROGRAMME

The main objective of the Microbes and Man Research Programme is to increase our understanding and knowledge of the interaction between host and microbes, and to apply this knowledge to the maintenance of health and prevention and treatment of diseases. The Programme aims to increase understanding of:

- the development, composition and health effects of the resident microflora under the influence of both host and environmental factors, including nutrition of the host and effects of individual food components
- the host-microbe interactions in the development and course of diseases and their sequelae
- the ways in which microbes and/or their metabolites in the environment influence human health

The research supported by the programme is expected to take advantage of the technological and knowledge bases of the postgenomic era. The programme will be seeking to generate multidisciplinary networks of microbiological research and to promote researcher training and exchange. International contacts are an integral part of both the research programme and the research teams involved.

The enhanced activity in basic research is expected to underpin the advancement of applied research. A further objective of the programme is to strengthen cooperation between universities and research institutes, and to facilitate the practical application of research findings.

Apart from scientists working in health research, biosciences and environmental sciences, the networks could also involve scholars interested in the historical, sociological and behavioural consequences of the improved understanding of microbes and their relation to man.

4 EXAMPLES OF RESEARCH THEMES

The interactions between the microbes and the host work as a rule in both directions, posing a special challenge to their study. The situation is further complicated by the fact that microbes on the mucous membranes and the skin are part of a complex microflora and receive messages from it. Likewise, human cells in contact with the microbes are subject to complex interaction with other cells in the body. Obviously, a multidisciplinary approach is necessary in order to advance knowledge in this area.

In recent years there has been an increasing realization of the significance of the interplay between microbes and man in the pathogenesis of disease. Virulence is not a single and solely microbial characteristics, but dependent on continuous host-microbe interaction. In fact, microbial virulence is only relevant in the interaction with a susceptible host, something which also affects the traditional definition of a pathogen. There is a paradox in that the microbes that belong to the normal microflora of mouth, intestinal tract, vagina, and skin (and which may be maintained by many unknown factors) in other cases may constitute our most common causes of disease. The mechanisms of such transformations are not known. The microbial ecosystem in the human body is continuously under influence of both internal and external factors, such as antibiotics and nutrients. As important is the complex role of our immune system, and our innate immunity. A variety of research questions addressing these problems are only now opening up for study with the powerful new technologies.

The role of microbes as etiological agents of non-infectious diseases has come under increasing attention during the last decades. Examples include the role of *Chlamydia pneumoniae* in cardiovascular diseases and the exposure to environmental and resident microbes in the development of allergic diseases.

The upper respiratory tract is the portal of entry of most of the viral and bacterial infections that continue to burden the health services, lead to often unnecessary use of antimicrobials, and cause loss of working time. The abundant microflora in this compartment is believed to play a central role in our natural defence against these infections both directly and through stimulation of local immunity. Pertinent research questions include the parameters of this defence and the combined effects of viral and bacterial challenge and the resident microflora.

The gastrointestinal tract is regarded as the most important metabolic unit in the human organism. However, our knowledge about the intestinal microflora is based on research dating back some 20-30 years. With the development of new research methods our focus will be turning to the growth and development of the intestinal microflora. The interaction between nutrition and microflora in the maintenance of health and in the pathogenesis of diseases is of global interest.

The development of foods with beneficial health effects (prebiotics, probiotics) and the development of animal fodders substituting antibiotics and growth hormone have important financial implications. However, the exact mechanisms that can explain how these products

work, still remain unknown. Basic research into the intestinal microflora will pave the way to applied research in this field.

The environmental microflora has much greater diversity than the human microflora. Exposure to environmental microbes and their metabolic products may have long-standing and significant impacts on human health. Human activity itself may have unexpected effects on environmental microbes, which are reflected back upon man. Apart from environmental microbes, the significance of the metabolites they produce with medical or other effects is an important area of research with major implications to human wellbeing.

The changing relation between man and microbes also involve many social, behavioural and historical aspects. An area of social interest is the role of microbes in the food production chain, including new cultivation methods such as organic farming that utilizes composted wastes and animal manure as fertilizer. Other economically and environmentally important areas, including severe health risks are related to water and waste management, and to buildings with mould and moisture damages.

5 IMPLEMENTATION OF THE PROGRAMME

The Microbes and Man Research Programme is scheduled to run for three years (2003-2005). Appropriations granted will be available in January 2003.

The programme will be implemented jointly by the Academy of Finland, the Swedish Foundation of Strategic Research, the National Technology Agency (Tekes) and the Finnish Work Environment Fund. The Board of the Academy of Finland has earmarked a total of EUR 4.1 million for the programme. Other funding bodies may allocate additional funds to projects which fall within their sphere of interest (see below: Research priorities of the funding bodies).

The Microbes and Man Research Programme will run parallel in Finland and Sweden and share common activities. The international collaboration and especially collaboration within the programme will be encouraged and can take many forms: joint research projects, cooperation within research networks, joint workshops, research visits and training.

The programme has a steering Programme Committee composed of representatives of the funding bodies. Members of the committee are Professor Marja Makarow, chair (Research Council for Health), Professor Annele Hatakka, vice chair (Research Council for Biosciences and Environment), Professor Juha Sihvola (Research Council for Culture and Society), Professor Timo Vesikari (Research Council for Health), Professor Pirjo H. Mäkelä (National Public Health Institute), Senior Technology Advisors Erja Heikkinen and Jari Toivo (National Technology Agency), Professor Olle Stendahl (Lindköping University) and Programme Manager, Dr. Elisabet Reizenstein (Swedish Foundation for Strategic Research). In addition, Dr. Olle Edqvist, Head of Planning (Swedish Foundation for Strategic Research) and Professor Hans-Wolf-Watz (Umeå University) and Scientific Secretaries Sirpa Nuotio, Tuula Aarnio and Maija-Liisa Toikka from the Academy of Finland participate in the work of the Committee. Programme Manager, Dr. Soile Juuti (National Public Health Institute) takes care of the scientific and administrative coordination.

6 RESEARCH PRIORITIES OF THE FUNDING BODIES

The funding bodies allocate part of their funding to such fields of research and development that are central to their own activities. Projects can be funded by one of the bodies or be jointly supported by any combination of them.

The Academy of Finland

The Academy of Finland is an expert organisation on research funding.

A research programme as defined by the Academy of Finland consists of a number of interrelated projects within the same target area of research. In funding such a programme the Academy of Finland seeks to raise the level of research in the field and to encourage a multidisciplinary and international approach to research. Other motives include developing and strengthening the knowledge base, bring together scattered research capacity, promoting professional careers in research and encouraging networking between researchers and reinforcing researcher training.

For further information on the Academy of Finland, go to www.aka.fi/eng. For more information on the Microbes and Man Research Programme, please contact: Ms. Sirpa Nuotio, Scientific Secretary, tel. +358 (0)9 7748 8360, sirpa.nuotio@aka.fi

The Swedish Foundation for Strategic Research (SSF)

The major objective is to promote the development of vigorous research environments of the highest international class and of importance for the development of Sweden's future competitiveness. This includes supporting and building up:

- international first-class research environments
- scientists with graduate degrees who through broadened and improved research training are attractive within industry, administration, and at research institutions
- research constituting a basis for the development of existing or new enterprises
- work resulting in increased employment opportunities, and improved working and health conditions
- research that acts as a focus for international cooperation of benefit for Swedish industry

SSF will launch a simultaneous programme in Sweden, which shares the general objectives of the Finnish programme. The main focus of the Swedish programme is to increase an understanding of the interaction between microbe and host - the microbiological ecology in the human body - and to apply this knowledge in the fields of prevention and treatment of human disease and/or maintenance of health.

For further information about the Swedish Foundation for Strategic Research and about the Swedish Programme Memorandum, please visit: www.stratresearch.se
or contact, Ms. Elisabet Reizenstein, Programme Manager, tel. +46 8 505 816 71

The National Technology Agency (Tekes)

The National Technology Agency is the main financing organisation for applied and industrial R&D in Finland. The main objective of Tekes is to improve the competitiveness of Finnish industry and service sector by technological means. In addition to industrial R&D grants and loans, Tekes provides funding to basic research projects at universities and research institutes containing innovative technological elements. Tekes participates in the Microbes and Man Research Programme in case applications that meet the Tekes funding and research programme criteria are filed.

More information is available on Tekes' website, www.tekes.fi, and from Ms Erja Heikkinen, Senior Technology Adviser, tel. +358 (0)10 521 5848, erja.heikkinen@tekes.fi or
Mr Jari Toivo, Senior Technology Adviser, tel. +358 (0) 10 521 5884, jari.toivo@tekes.fi or
Ms Liisa Rosi, Senior Technology Adviser, tel. +358 (0)10 521 5794, liisa.rosi@tekes.fi

The Finnish Work Environment Fund

The Finnish Work Environment Fund finances research and development work, which improves the working conditions and promotes the safety and productivity aspects of the working place activities. Research teams can apply funding from the Work Environment Fund within the Microbes and Man Research Programme.

Good research takes a multidisciplinary perspective on its subject, and in this respect new openings are more than welcome. Research that extends all the way to the individual workplace helps to establish whether theoretical ideas have real practical applicability in promoting occupational and health safety aspects. It also provides a sound foundation for comparisons and evaluations and further for drawing conclusions that have immediate relevance to the everyday working life.

For further details on the Finnish Work Environment Fund, go to www.tsr.fi or call +358 (0)9 6803 3311, or contact Ms Riitta-Liisa Lappeteläinen, Director, tel. +358 (0)9 6803 3312, riitta-liisa.lappelelainen@tsr.fi.

7 APPLICATION PROCEDURES AND DEADLINES

First stage: deadline May 27, 2002

Applications for participation in the programme will be processed in two stages. In the first stage, **plans of intent** shall be submitted **by May 27, 2002 (before 4.15 pm).** The plan of intent shall be prepared either by using the Academy of Finland's electronic services on the Academy's website www.aka.fi/eng or on the Academy of Finland application form SA 1.2002E, with the programme acronym ´MICMAN` indicated on the first page. All documentation shall be completed **in English**. When a printed version of the application form is used, **20 copies** of all application documents complete with appendices shall be submitted to the Registrar's Office of the Academy of Finland.

The application form shall be filled in accordance with the guidelines of the Academy of Finland (see the Guide for Applicants) with the exception that the only appendices to be submitted are:

- a plan of intent of no more than three pages in length (Times Roman or related, 12 pts), including the references
- the CV of the principal investigator of no more than two pages in length
- a list of no more than 20 key publications of the applicant.

The plan of intent shall briefly describe
- the research problem and the objectives
- the research plan and the main research methods
- the researchers involved and resources available
- possible international research collaboration
- budget outline and timetable

If the applicant is a **consortium**, only one plan of intent shall be prepared. The share of work undertaken by each partner and the total collaborative effort and the added value gained from the project is to be described in an additional page. ~~The leader of the consortium shall prepare one application form on behalf of the whole consortium. In addition,~~ Each team leader of the consortium shall include his/her own application form, CV and a list of publications.

In the first application stage, principal investigators in Finland shall direct their applications primarily to the Academy of Finland and principal investigators in Sweden primarily to the Swedish Foundation for Strategic Research. Applications will be evaluated jointly by the participating funding bodies, and the applicants will be informed in writing about the decisions by the end of June 2002. Those principal investigators that will be invited to file full-length applications will be informed to which funding body or bodies they should address their full applications. Projects can be funded by one of the bodies or be jointly supported by any combination of them.

Second stage: deadline September 2002

The full applications shall be submitted by September 16, 2002 (before 4.15 pm). Applications shall be prepared either by using the Academy of Finland's electronic services on the Academy's website www.aka.fi/eng or on the Academy of Finland application form SA 1.2002E, with the programme acronym ´MICMAN` indicated on the first page. All documentation shall be completed **in English**. When a printed version of the application form is used, **20 copies** of all application documents complete with appendices under one cover shall be submitted to the Registrar's Office of the Academy of Finland. The application form shall be filled in accordance with the guidelines of the Academy of Finland (see the Guide for Applicants).

Applications will be evaluated by an international panel of experts on the following criteria:
- compatibility with the programme objectives
- scientific quality and innovativeness of research plan
- feasibility of research plan
- competence of applicant /research team
- national and international collaboration
- researcher training and advancement of research environments

The call for proposals to this programme, application forms and the Academy Guide for Applicants can be obtained from the Academy of Finland's website at www.aka.fi/eng and from the Registrar's Office, where applications should also be returned.

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Further information also available at:

www.aka.fi/eng > Research Programmes > Research Programmes to be started in 2002
or
www.aka.fi/tutkimusohjelmat > Vuonna 2002 käynnistyvät tutkimusohjelmat