FUGE – Functional genomics in Norway

– a national plan

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Foreword

During the past year, various circles have called for Norway to increase its focus on functional genomics, in keeping with developments in various other western countries. SAMGEN, an agreement of intent between the University of Oslo, the Agricultural University of Norway and the Norwegian School of Veterinary Science, is one of several initiatives supporting this view.

As a result of strong interest within the research establishment, the Research Council of Norway hosted a meeting to discuss whether it would be possible to draw up an overall plan for the nation as a whole. This meeting, which took place in Oslo on 3 November 2000, was attended by some 70 researchers, research directors, directors of institutions and other resource persons. A national committee was appointed and charged with the task of preparing a national plan for functional genomics research in Norway.

The committee had one representative from each of the four main regions: Jan Trulsen from the University of Oslo, Vidar Steen from the University of Bergen, Ole Jan Iversen from the University of Science and Technology in Trondheim, and Georg Sager from the University of Tromsø. Chaired by Geir Stene-Larsen from the Research Council of Norway, the committee has established extensive local contacts within each region, and its recommendations to a large degree incorporate input from those who are working directly within the field, and who therefore best know its future needs.

FUGE is the culmination of the committee's efforts. At a meeting held on 16 January 2001, it was confirmed that the plan has received broad-based national support. Devised by research institutions, FUGE is based on the views of the research community, and it is a proposal endorsed by a unified Norwegian research establishment.

FUGE is presented in three documents: a summary, the present main document and a compilation of supplementary background notes. These documents have been designed to be easily accessible to a wide audience, and no special knowledge is required to be able to understand the substance.

As stated in the following pages, the plan is based on an underlying desire to introduce better modes of interaction between the research establishment and trade and industry. Although much remains to be done vis-à-vis this process, representatives of trade and industry have already indicated that FUGE is a measure that will also clearly benefit the private sector.

This document provides an outline of the most important elements of the organizational model. Further details will be presented in the spring, at the latest by 1 May. Until that time, the national committee will serve as the coordinating secretariat for FUGE.

FUGE will be submitted to the political authorities on 25 January 2001.

Oslo, 20 January 2001

1 Introduction and main points

Knowledge about genes and their products has become increasingly important in research, medical and industrial circles. Norway will be unable to compete on the global market of the future unless there is considerable investment in research within this area. Over the next 5-10 years, annual allocations of a minimum of NOK 300 million will be needed to finance research in the field of functional genomics.

This proposal to enhance research in functional genomics has been submitted by a unified Norwegian research community. The proposal outlines the allocation of responsibilities at the national level, the identification and utilization of national advantages, regional cooperation, the design of new models for interaction between universities[1] and research institutions on the one hand and trade and industry on the other, and measures to systematically strengthen the priority areas specified in Report to the Storting No. 39 (1998-99), *Forskning ved et tidsskille* (*Research at the beginning of a new era*).

The research of the future

The successful mapping of the genomes of humans and certain animals, plants and microorganisms has opened new doors for scientists studying biological processes. Landmark technology has made it possible to study tens of thousands of genes and proteins simultaneously. The field of functional genomics utilizes these methods to determine the functions of the genes and proteins and the ways in which they affect one another.

Research in this field will provide new insight into how biological processes function. This understanding will form the basis for pharmaceutical products to combat diseases that are presently incurable and new methods in agriculture and aquaculture that will increase the food production output, as well as methods to neutralize environmental toxins.

Technology of the future

- Increasing Norway's research capacity in functional genomics may be a means of ensuring future productivity as national petroleum and gas reserves gradually become depleted.
- In coming years, competition on the international market will continue to increase. Norway must work fast now to obtain the high-tech expertise needed to remain internationally competitive.
- The number of new enterprises focusing on IT, biotechnology and functional genomics is quickly rising. Many of these are materializing in close connection to universities that conduct high-level basic research. The economy of tomorrow dictates that proximity to – and organized liaisons with – large-scale, creative educational centres will be a must for emerging companies.
- Norway should immediately initiate activities to establish similar mechanisms.

Future impact on society and industry

Today, the applications of biotechnology are reaching into areas that were unimaginable only a few years ago. Internationally, many countries are giving priority to strengthening

[1] The term universities is used to refer to the four national universities together with the Agricultural University of Norway and the Norwegian School of Veterinary Science.

research activities in this field: Sweden has allocated an additional NOK 1.2 billion for national research efforts over the next five years; Ireland has allocated NOK five billion; the USA, Japan and a number of countries in Europe are all greatly intensifying their activities.

Increasing Norwegian research capacity in functional genomics is also a prerequisite for further development in the marine resource sector, for providing tomorrow's patients with health care services equal to those available in other countries, and for enabling Norwegian universities to recruit and supply the expertise that will be needed in future research and industrial development circles.

Objectives:

- *Basic biological research.* FUGE is intended to bring the level of the basic research disciplines underlying functional genomics up to international standards. Furthermore, Norway will work to develop cutting-edge expertise in areas of particularly strategic importance, or in which the country has special advantages.

- *Medical research.* FUGE will help to make it possible for Norwegian health care services to utilize the new knowledge and medical products that result from functional genomics, thus ensuring that Norwegian health care remains on a par with top-quality services available elsewhere in the world.

- *Marine research.* FUGE will play a role in establishing the research basis needed to promote further development of the aquaculture industry, optimal utilization of marine resources, and the creation of a biomarine industrial cluster in Norway.

National distribution of responsibility

It is essential that basic expertise in functional genomics be established in all regions in Norway. FUGE provides recommendations for delegating responsibility to the various regions and among the various participating bodies within the regions.

Regional cooperation

FUGE will set up a system for regional cooperation that integrates universities, institutions, colleges and trade and industry within subject areas that are relevant to functional genomics.

Industrial development

In future, most industrial innovation will be rooted in research. The new industrial sector will be dependent on both the know-how and the commercially viable ideas that can only be generated from basic research activities. FUGE will make every effort to ensure that the focus on functional genomics research is designed to boost Norwegian industry. It will be essential to devise constructive models that facilitate interaction between industry and academia in this area.

Cooperation with top researchers abroad

If efforts to raise Norwegian research to international levels are to be successful, then top researchers from abroad, with broad-based international networks, must be encouraged to come and work in Norwegian laboratories, and Norwegian researchers must be prepared to travel elsewhere and learn from the leading research communities in other countries. Norwegian efforts in this field should be linked to activities taking place in the other Nordic countries.

Ethical issues

Like any other technology, the powers of biotechnology can be used and abused. Thus it is important to ensure that all research conforms to the ethical principles underlying the Norwegian culture. FUGE will therefore foster a strengthening of research on the ethical, legal, environmental and safety aspects of functional genomics.

Organizational model

FUGE will establish an administrative system for distributing NOK 300 million annually to intensify top-level research in functional genomics, to create the necessary infrastructure as regards high-cost equipment with appurtenant personnel, and to recruit and train the research personnel that will be needed.

2 Why do we need functional genomics?

Basic biological research

Years of basic biological research, combined with the emergence of new technology, have paved the way for contemporary genomics. Much of the 21st century's cutting-edge research in the natural sciences, medicine and technology will be based on some type of functional genomics. Basic and applied research will be closely interconnected. New techniques are rapidly evolving, and technologies that were considered science fiction a few years ago are now established research tools that have already been applied in a number of areas.

Functional genomics will have an impact on most of the biosciences, and the new technology will stimulate renewal of the research establishment. Fields such as cellular biology, botany, zoology, ecology, microbiology, biochemistry and genetics will be greatly transformed. Functional genomics will need to integrate aspects of a number of other disciplines, such as chemistry, informatics, physics and mathematics. This field will also have relevance for disciplines such as philosophy, law, ethics and the social sciences both directly and indirectly.

Basic research provides the foundation for applied research in medicine, agriculture, aquaculture and the processing industries. Thus it is essential that basic research is sound and up to international standards. The gap between basic and applied research is steadily decreasing, as new knowledge is more rapidly being translated into practical applications. In order to be able to compete in the applied research sphere, Norway needs to substantially upgrade and renew the basic research being conducted at universities and research institutes. Investment in research within functional genomics will also be required in order to succeed in the priority areas specified in Report to the Storting No. 39 on research at the beginning of a new era.

FUGE will enable Norway to implement the innovation and restructuring within basic biological research that is needed to be in the forefront of international developments in research.

The health care of the future

Internationally, developments in medicine are spurred by two technological "engines": information technology and biotechnology. Progress in each of these fields benefits the other, fuelling further advances in various medical fields in the years to come. Functional genomics is a collective term for the research that will emerge in the wake of the mapping of the human genome. This research will provide radical new insights into how biological processes function, and it will generate substantially simpler, quicker, safer and better methods for diagnosing and preventing disease. It will also make it possible to treat diseases that are presently incurable, or for which current treatment is inadequate – and to tailor treatment for the individual patient, enhancing its effectiveness and reducing the side effects.

Knowledge of the function of genes will yield entirely new medical insights in a number of fields. Textbooks will need to be rewritten, and the physicians of tomorrow will need to possess a different type of competence than that of their present-day counterparts. Thus the system of education will also need to be changed. In order to achieve this, Norway must promote extensive, independent research efforts in this field.

The challenge facing us in the coming years will be to link insight into gene function with clinical efforts. This will be essential if health care personnel in Norway are to be able to use the many new medical treatments that will become available.

FUGE will help make it possible for Norwegian health care personnel to use the new knowledge and medical treatments generated by functional genomics – and to address the attendant ethical problems – so that the population may continue to enjoy health services on a par with the best elsewhere in the world.

Biomarine industrial cluster

The export value of fisheries and fishery products was approximately NOK 33 billion in the year 2000, but the potential is much greater. Estimates indicate that the export value may reach NOK 150 billion by the year 2020. Growth in the marine-based industries may become one of the most important components in the Norwegian economy as oil revenues gradually stagnate and decline. However, these opportunities can only be realized if we succeed in stepping up the research required to solve the problems we are facing.

New pharmaceutical products

- Many pharmaceuticals work by affecting one or more of the body's proteins. Thus far the mechanisms that underlie such treatment are known for only about 400 of the body's proteins.
- The potential in this area is enormous. Human genetic material contains somewhere between 40 000 and 100 000 genes. Each of these genes can produce one or more proteins which have various functions in the body. These may cause disease if they do not function as they should, and they may thus provide the basis for new pharmaceuticals.
- Functional genomics is now widely used to develop new pharmaceutical products based on knowledge about these genes and proteins. Modern robot technology is greatly utilized in these efforts.
- Many of our most common diseases are caused by interaction between several types of genetic defects and environmental influences. Cancer, cardiovascular disease, diabetes, Alzheimer's disease and schizophrenia are examples of such multifactorial diseases. In the future, functional genomics may make it possible to identify the cause of diseases that are related to defects in a number of genes.
- In recent years leading international research groups – with Norwegian participants – have demonstrated that functional genomics can be used for high-precision diagnostics and classification of cancers such as leukemia and breast cancer.

Food and health

- Our own health depends on the nutritional and health status of animals and plants. Functional genomics will help us understand these connections.
- Insight into the genetic material of viruses and bacteria may lead to highly effective methods of identifying contaminated food. The "Safe Food" programme may reduce the incidence foodborne diseases and toxins.
- Functional genomics may become a vital tool in the fight to curtail antibiotic resistance, which is a growing problem internationally.

At present, Norway has the best salmon breeding stock in the world, but this advantage will soon be lost if we do not redouble our efforts to improve characteristics such as growth rate, feed utilization, flavour and colour. Disease is a persistent problem for fish farming operations. But perhaps the greatest problem of all is the shortage of fish feed. Insufficient supplies of feed with the appropriate fat composition will soon prevent further growth in the industry. Thus the opportunity may present itself for both agriculture and other industry to produce fish feed of the required quality and composition. Functional genomics holds the key to breeding, feed production and the prevention and treatment of diseases in fish and shellfish.

International competition will continue to grow increasingly sharper. In order for Norway to be able to compete in the long run, it should be a national goal to develop a biomarine industrial cluster.

A biomarine industrial cluster will need to include several major players: food producers (the fish farming industry, breeding organizations, the fish feed industry, the food processing industry and an appurtenant logistics industry), biotechnological industry (a growing number of small and medium-sized biotechnology companies with top-notch professional know-how), pharmaceutical enterprises and equipment suppliers. Functional genomics will provide the basis for these activities. It will supply industry with the ideas that can be patented, the personnel that has the required competence and the production technologies that are needed.

Research fields results

- The Norwegian firm Norferm AS has harnessed a species of bacteria which "consumes" natural gas from the North Sea and transforms it to a biomass that has been approved for the production of feed for fish and animals.
- Biotec ASA is a research-based marine biotechnology company. Established by researchers from the University of Tromsø in 1990, it produces biochemical substances from naturally occurring marine products and converts them into products that can be used in food, feed and medicines. Eighty per cent of the production is exported, mostly to the USA and Japan.
- Biological substances extracted from marine and land-based organisms may have many valuable medical applications. Bioprospecting is a new field which aims to exploit these possibilities. Norway, with its long coastline and geographical location, has unique advantages here.

In the future, bioprospecting may become an important source of new discoveries and inventions. Bioprospecting is the search for commercially viable molecules in nature, including the mapping of the genomes of organisms that are of economic interest. Mapping of the salmon genome is an area where Norway is already a world leader. In order to safeguard present and future industrial interests, it should be a national goal for Norway to maintain its lead in the exploitation of the salmon genome.

It is of particular interest for Norway to conduct bioprospecting in the Arctic regions, where aquatic organisms have adapted to life under extreme conditions since the beginning of time, but there may also be reason to extend this activity to land-based organisms. An important aspect of bioprospecting is to preserve biodiversity and to acquire an understanding of the traits that provide natural resistance to disease and harmful environmental influences.

Research in this area has already been established in Norway, and the first enterprises have been launched.

For generations, microorganisms from nature have provided the basis for vital industrial processes and products. It is estimated that less than 0.1% of all the species of microorganisms that exist in nature have as yet been isolated and described. Thus microorganisms represent a vast potential for new processes and products. Research in the past decade has uncovered a rich flora of bacteria that live in extreme conditions, such as high or low temperatures or under high pressure. The traits which make this possible can be exploited in research and perhaps provide the basis for new products.

Commercialization of discoveries from bioprospecting or from the exploitation of waste products from the fisheries, agricultural and foodstuffs industries will find applications primarily within human and veterinary medicine, but also within the fine chemicals industry.

FUGE will help Norwegian marine industry to prosper in the sharply competitive international climate and provide a foundation on which Norway can establish a biomarine industrial cluster. FUGE will make it possible to exploit Norway's coastal resources in the broadest sense – everything from traditional aquaculture to systematic searching for new biological material that is found in animals, microbes and plants.

The industry of the future

Biotechnology, which has long been one of the strongest driving forces behind the international industrial sector, already comprises a vital part of the modern economy. In coming years, however, it is expected to assume an even more pivotal role. Some financial analysts believe that as much as 70% of all land-based industry and 40% of the total economy will be based on some type of biotechnology twenty years from now.

The production of chemicals, agricultural products, pharmaceuticals and various products in the processing industries will utilize methods from biotechnology. Polluting industrial smokestacks will be replaced by "clean" biochemical processes in enclosed rooms; complicated machines will be replaced by simple biological systems; products that are now manufactured in factories will be

Biotechnology enterprises – the new economy

- The consultancy firm Cap Gemini Ernst & Young recently conducted a study of Norwegian biotechnology industry. They concluded that, compared to other western countries, Norway has a relatively large number of biotechnological enterprises in relation to the size of the population. However, these enterprises are for the most part small and under-financed, with a slower growth rate than their foreign competitors.
- Internationally, there is a strong trend in the biotechnological industries to establish geographic centres that attract capital and labour. Norway should aim to create similar self-reinforcing effects within the industry, both by establishing viable Norwegian centres and in collaboration with the industrial centres in our neighbouring countries, such as in the Gothenburg-Lund-Malmö-Copenhagen region.
- The Confederation of Norwegian Business and Industry (NHO) has established a Forum for Biotechnology to strengthen Norwegian biotechnological industry.

produced by agriculture. Without access to this know-how, Norwegian industry will find it difficult to compete just a few years from now.

Biotechnological research has been emphasized in Norway during the past decade or two, both at the universities and within industry. This has given Norwegian biotechnology enterprises access to essential know-how, enabling them to develop the research-based products that are needed to be able to compete internationally. Largely thanks to these efforts, it is now worthwhile to undertake further development of biotechnological industry in Norway.

However, in light of the competitive pressure facing this industry, these efforts have been far from adequate. Compared to other countries, the industrial base for biotechnology in Norway is weak. Substantial investments are needed if Norway is to be in a position to take advantage of the vast potential this sector represents.

Increasing competition in the food market means escalating demands for know-how throughout the entire value-added chain, from primary production to the food processing industry, for both fishery and agricultural products. Functional genomics will be able to provide key knowledge for producing safe food, for developing food with beneficial health effects and for developing feed for livestock and fish. Consumer awareness of safe, healthy food means increased demand for food that contains beneficial bacteria, antioxidants, and the appropriate fatty acid and fibre components, and that can help reduce the incidence of life style diseases. Internationally there is a large and growing market for food with beneficial health effects. Foods with such qualities will be able to compete in other areas than price. Norway should have the prerequisites needed to take part here.

Functional genomics can provide a forward-looking basis for production and the development of new jobs in a number of areas where this technology is not applied at present. Internationally, the biotechnology enterprises of the future will largely be established near major institutions of research and education.

Some national advantages

- Biobanks. By linking information from medical biobanks (biological material collected during health screening and surveys or during patient treatment) with information from population surveys, it is possible to investigate how genetic factors and environmental influences affect disease and health. In part because we have a number of registers that do not exist in other countries, Norway is in a unique position internationally in relation to this type of research. The potential for utilizing these and other sources of data is tremendous. For instance, there are hospital biobanks that have stored test material from four or five generations of patients. Norway's biobanks may prove to be a veritable gold mine for research.
- Marine model organisms. The diversity of marine organisms is nearly unfathomable, and many species have not yet been discovered or sufficiently mapped. Functional genomics using marine organisms as model organisms may generate entirely new knowledge relating to genes and proteins that is relevant for the development, growth and health of humans, animals and plants. Norway has great potential to succeed in this sphere internationally.
- The salmon genome. Norway is already the world leader in breeding farmed salmon. This may provide a vital competitive edge in the work of mapping the salmon genome. Knowledge about the genes of salmon will have major significance for the fish farming industry.

Norway should aim to build up similar systems for collaboration between academia and industry, where innovative ideas, cutting-edge competence and industrial clusters can be developed in close networks. The industrial sector will play a major role in providing the impetus for both basic and applied research in this context.

A primary objective for FUGE is to develop Norway's national expertise in basic functional genomics. FUGE also represents a long-term investment in Norwegian industry. Thus it is an important task to create viable models for collaboration between industry and academia in this field.

FUGE will play a role in developing the expertise needed to ensure that the biotechnological and processing industries are equipped to meet future requirements for technology. FUGE will also encourage the development of new mechanisms for collaboration between research groups and industry in order to create better conditions for new business ventures.

The environment of the future

Protecting our ecosystems is one of the pillars of environmental efforts. Functional genomics can provide new insights into the interplay between species and the effects of environmental factors, which in turn will make us much better able to safeguard the diversity that exists in nature.

Functional genomics can help reduce the extent of pollution, in part by improving production processes so that they require less energy and discharge smaller amounts of environmentally harmful emissions, and in part by developing products that are more environmentally friendly. For instance, biodegradable plastics can be developed from biological waste products, or disease-resistant plants can be bred, so that spraying them with chemicals is unnecessary.

Functional genomics can be used to detect pollution, for instance by finding microorganisms with "signal genes" that are activated in the proximity of environmental toxins. Such technology can make it substantially easier to monitor the quality of water and air, identify emissions of environmental toxins and manage our biological resources in a responsible manner. Functional genomics can also be

Functional genomics and the environment

- To what extent can modified genes *establish* themselves in nature through transfer from one individual or species to another? How are local organisms and ecosystems influenced by new genes in their surroundings? We need research to investigate these and other key environmental issues.
- The Norwegian company Biosense Laboratories AS is a leading manufacturer of testing systems that can identify foreign substances and toxins in foodstuffs, pharmaceuticals, chemicals and water. Their products are used worldwide to monitor environmental pollution and food safety. Products from Biosense Laboratories AS have made it possible to detect pollution at a very early stage.
- Functional genomics will be an important instrument in future agricultural research to ensure good animal and plant health and high food quality and to ensure sustainable utilization of natural processes in feed production.

used to clean up pollution, for instance by developing oil-consuming bacteria or microbes to break down specific environmental toxins that are difficult to deal with at present, or plants that can extract heavy metals from the soil.

In the future, proper environmental documentation will provide industrial enterprises with a substantial competitive advantage. It will be of great value to the commercial sector to determine which areas are associated with such a high degree of environmental risk that investments are not advisable. Functional genomics may prove an important tool in this arena.

As always when dealing with any new technology, there are potential dangers associated with biotechnology. Throughout the world, widespread research is being conducted to improve characteristics of plants and animals by altering their genes. Releasing gene-modified organisms (GMOs) in nature may influence ecosystems in ways we cannot predict at present. To deal with this successfully Norway will need high-level national research – both to acquire the know-how needed to use the findings from other countries, and because research results from other countries are often not directly transferable to Norwegian ecosystems and natural surroundings.

Safety is cardinal. Only targeted research investigating potentially harmful effects on health and the environment can enable us to utilize the positive aspects of biotechnological research while avoiding the negative ones.

FUGE will play a role in making functional genomics a useful tool for environmental efforts and in ensuring that Norway acquires sufficient knowledge of the possible harmful effects of biotechnology for health and the environment to enable us to utilize the positive aspects of this powerful technology while avoiding the negative ones.

The ethical aspect

Biotechnological research opens up unprecedented opportunities for acquiring new knowledge. This makes it possible to cross thresholds that were previously insurmountable. Functional genomics will generate a number of valuable new products such as medicines to combat diseases that are incurable at present, new methods that make it possible to increase the food production output of agriculture and aquaculture, and new methods for neutralizing environmental toxins. At the same time, functional genomics may also provide us with the capacity to affect nature adversely.

Ethical issues

- New knowledge about the functions of genes may change our understanding of nature and humankind. How will this influence the way in which we address disease, social problems and the non-human elements of nature?
- How shall we deal with knowledge that may be used to predict our fate, for instance by identifying the risk of future disease?
- How will research influence relations between wealthy nations, who can afford to conduct their own research, and poor nations, who are not able to benefit from this technology? How should we address the "genetic theft" from poor developing nations by major research nations?

As is the case with any other powerful technology, biotechnology can be used or abused. The greater the risk that we will not be able to prevent future abuse, and the greater the risk of unforeseen effects of biotechnological research, the more important it is to ensure that the research conducted is consistent with the ethical principles on which we wish to base our culture. A national programme for functional genomics must thus have a considerable focus on research into the ethical and legal aspects of functional genomics.

Functional genomics will continue to advance, presenting new ethical dilemmas to which we do not have the answers. Responsible research groups should be established that will be able to advise and supply necessary information to politicians and other decision-makers in Norway, enabling them to make sound decisions regarding the use of these new opportunities.

A number of research groups and individual researchers in the humanities, law and the social sciences are currently conducting research on ethical, legal, philosophical, social and cultural aspects of functional genomics. Thus it will only take a short time to build up substantial expertise in these areas if sufficient funding is made available.

FUGE will facilitate the development of national research expertise to ensure that functional genomics conforms to the ethical principles underlying the Norwegian culture.

3 What expertise do we need?

From genetic structure to genetic function – functional genomics

Human genetic material (DNA) contains somewhere between 40 000 and 100 000 genes. Soon we will have an accurate map of these genes, with access to detailed information about the structure of the individual gene. Likewise, the DNA has been decoded for several other genetic model organisms, including the nematode worm, the fruit fly, thale cress (*Arabidopsis thaliana*), the yeast cell and nearly 50 species of bacteria – and similar information will soon be available to describe mice, zebrafish and rice.

The recipe for life

- The genome – the complete genetic material with all the genes – contains all the information that is needed in order for an organism to exist, whether a person, animal, plant or microorganism.
- Each of the genes contains the recipe for how one or more proteins can be produced in the cells. The role of the genes is to ensure that the right proteins are produced in the right cells at the right time.
- The proteins have many different functions in an organism: as enzymes that catalyze chemical processes in the cells, hormones that influence various bodily functions, immune substances providing defence against infections, or building blocks in various types of tissue.
- The way in which genes and proteins interact determines the characteristics of an organism, and whether it is healthy or diseased.

The next challenge is to identify the functions of the genes. Genes express the biological traits of humans, animals, plants and microorganisms. The acquisition of new knowledge about genes will make it possible to identify, prevent or treat disease in humans, animals and plants.

Functional genomics is a field that has developed in the wake of genome research. Using new technology, it is possible to study tens of thousands of genes and proteins at once. Thus it has become a realistic objective to determine how the genes and proteins in an organism function, both alone and in interaction with one another.

Functional genomics normally requires knowledge of the structure of a great number of genes. In order to gather this information, a vast number of genes must be examined systematically. The technique used is called DNA sequencing. Special machines (called sequencers) and techniques have been developed to perform this decoding on a large scale. When the DNA for an organism in its entirety is mapped out using this method, it is called genome sequencing. However, knowing how genes are constructed is not sufficient to be able to fully describe their structure; it is equally important to know how the genetic material is organized. This is a very demanding task.

In order for a gene to make a protein, it must be active or “switched on”. Individual genes can be “switched off” or “switched on” under different conditions. In order to be able to use genetic knowledge, for instance to make pharmaceuticals for people and animals, to improve the resistance of plants to organisms that cause disease or to climatic stress, or to produce vaccines

against viruses and bacteria, we must know how genes work together and in what situations they are switched on or off. This is a cardinal task for functional genomics.

Although the human genome and the genomes of a number of model organisms have now been mapped, the task remains for a number of other organisms. Vital areas of research related to aquaculture and agriculture must begin by mapping the structure of the genes in the organisms to be studied.

Genetic similarities

- An important discovery was that most of the various organisms' genomes were maintained intact during evolution. This similarity in genetic makeup means that the findings from genetic studies of one species can often be transferred to others.
- In order to find new approaches for treating disease in humans, then, it is advisable to examine the relevant processes in organisms that are easier to study, such as the nematode worm, the fruit fly or mice, before embarking on the development of pharmaceuticals for humans.

From gene to protein – proteomics

Most genes code for and work through proteins. Proteins may have a wide variety of functions in an organism. Thus it is of great significance to know how proteins function. The complete profile of proteins expressed in a cell is called the cell's proteome. There are thousands of different proteins in each individual cell, and different types of cells contain different sets of proteins. The objective of proteomics is to discover how these proteins function and interact with one another.

Genes and proteins both influence each other. Some genes and proteins only work if other genes and proteins are also present. In other cases, genes and proteins may have a negative impact on one another. It is essential to know how genes and proteins interact in order to understand how genes actually function.

In order to determine the effect of proteins, it is necessary to know their composition; i.e., the way in which their components are arranged. It is also necessary to know the form that they take, i.e., their three-dimensional structure. Most proteins are coiled in a particular way and can only fulfil their function if they assume the correct three-dimensional structure.

Techniques have been developed for visual imaging of proteins, but determining protein structures is technically demanding. Data have been stored for a couple of thousand different protein structures in an international database (the PDB database), but the three-dimensional structure for most of the proteins has not yet been determined. In many cases only parts of these proteins' structures have been determined, perhaps only the biologically active part.

From genes to individuals – experimental models and epidemiological registers

Functional genomics investigates the relationships between genes and traits of humans, animals, plants and microorganisms. Which genes are active under various conditions? How are traits influenced by variations in the genes? What

changes in genes cause disease? What changes yield good health or desired traits?

Functional genomics implies a transition from studying a single gene or a single protein at a time to studying many genes and proteins at once. In nature it is precisely this interplay among many factors that is significant. Thus functional genomics represents a major advance in relation to earlier laboratory research, which was often able to study only one factor at a time.

This technology gives us entirely new opportunities to study how genes influence the traits of an organism. This often requires using some type of experimental model: a laboratory animal, a cell culture or a test plant, in which it is possible to observe the changes that take place when specific factors in the environment or the genes are altered. For instance, plants and laboratory animals have been developed in which one or more genes have been "switched off" (among so-called "knock-out" mice) or "switched on", making it possible to study the function of these genes in an organism.

Studies of how genes are regulated are a vital aspect of functional genomics. Whereas previous research has revealed simple genetic functions, functional genomics allows us to study how a large number of genes and proteins are regulated simultaneously through a network of signals that are intricately interlinked. In order to study such complicated interaction, high-capacity methods are often used, i.e., methods which make it possible to investigate a large number of genes or gene products in a single experiment.

Information on health, disease and biological functions can also be acquired by studying the incidence of disease (or other characteristics) in a group of people, animals, plants or microorganisms. Veterinary medicine uses breeding data and progeny records, while human medicine employs biobanks and health registers.

A biobank is a collection of biological material – for instance blood tests or tissue samples – from many persons or animals. A health register is a systematized collection of information on factors that may be significant for the individual's health. By comparing the information in such "databanks" with "databanks" for genes, it may be possible to find out what genes are involved in different conditions. Norway's unique collections of this type of data – for humans, farmed fish and livestock – represent great scientific and industrial potential.

Processing vast amounts of data – bioinformatics

Although genome data is available to everyone and can be analyzed using standard computers, powerful computers and advanced software are needed in order to analyze the information about genes and proteins in its entirety.

The amounts of data that must be developed experimentally in functional genomics are normally vast, indeed so vast that even the most powerful computers and advanced software are not able to analyze the collected genome

data in detail. At the same time, most of the data will not be of interest for the relevant research task.

The problem is that it is not clear at the outset which data are important and which are not. Searching for specific expressions in a vast amount of data, or more generally sorting out valuable information among the "slag" (data mining), places great demands on the information technology methods employed. Only an interdisciplinary approach – enlisting the collaboration of biologists, medical researchers and IT specialists – can succeed.

In addition to processing vast amounts of data, mathematical models must also be developed to simulate what happens in complex biological systems. This requires both research and cutting-edge expertise in the disciplines involved.

Efforts to develop more effective ways of processing genome-related biological data are taking place in the field of bioinformatics. Researchers have access to a number of bioinformatics tools via open websites. However, access to advanced expertise in bioinformatics is required in order to pursue certain types of functional genomics.

Vast amounts of data

- The information in the human genome (the complete human genetic material) is like an unbroken string of repeated combinations of four different letters, without any commas, full stops or spaces. If this string of letters were to be written out on paper, it would fill a stack of books one hundred metres high.
- If just one letter in this string of three billion letters is changed at a critical location, the individual will not be viable.
- The task of studying unknown gene changes is like gazing out over a huge metropolis after nightfall and looking for the one dark window that should be lit, and the one lit window that should be dark, without knowing which windows you should be looking for.
- Norwegian firms have the potential to make important contributions in this field. For instance, it appears that the technology developed by the Norwegian IT enterprise FAST may be useful in biological research.

As it is not yet practically feasible to determine the structure of all proteins experimentally, one branch of bioinformatics is dedicated to predicting protein structures. Using the methods available at present, it is possible to make predictions of acceptable quality only if the structure of a related protein is known. Thus research is needed to develop new and better methods in this area.

Bioinformatics is needed in order to process information about genes, proteins, and traits of laborabory animals or groups, as well as for processing the wealth of information that is required to be able to produce images of genes, proteins, cells and tissue. Thus an essential goal is to bring the level of the infrastructure and research in bioinformatics up to international standards and to ensure that Norway educates enough bioinformaticians for future needs.

4 Norway and the rest of the world

Norway has a lot of catching up to do – but also great potential

For years our neighbours have invested considerably more in biological research than Norway has. For instance, Sweden has spent three times as much per capita on medical research compared to Norway, Denmark twice as much – and the USA *ten* times as much.

Many countries are substantially intensifying their biological research efforts. The United Kingdom, Germany, France, Finland, Japan, the USA and a number of other Western countries are funding ambitious programmes in functional genomics. Ireland alone has set aside NOK six billion for this type of research in the coming five years. Sweden is planning to allocate NOK 1.2 billion and Denmark a similar amount. In the USA each of the major universities has been granted several billion NOK to foster this research.

The international experts who recently evaluated all bioscience research in Norway concluded that on the whole Norwegian biological research is below international standards. However, a number of individual researchers and research groups are on a par with the best in the world, and it will thus be possible to upgrade our research community if a concerted effort is made. The international experts were most surprised at the overall low volume of Norwegian biological research. Investments in this type of research will provide a basis for the most important growth areas in the medical science and industry of the future. Thus such investments must be regarded as necessary expenditure for future earnings.

Evaluation of Norwegian research shows that Norway lags far behind other countries

- Comparative international surveys show that Norwegian genome research has considerably lower penetration than that of the other Nordic countries.
- Norway also lags far behind the world average in both the number of scientific publications per capita and the penetration of the individual publication.
- An international expert panel which recently evaluated Norwegian biological research recommends that Norway should develop research groups for functional genomics and proteomics of a scientific calibre that can compete among the very best internationally.

5 The National Programme Plan

What is FUGE?

FUGE is the result of an initiative taken by the Norwegian research establishment; the underlying process has been supported by the Research Council of Norway. FUGE represents a cooperative effort between Norway's universities and research institutions and the industrial sector. The field of research involved, extending across many different disciplines, has been described as a marriage between biology, medicine and informatics.

FUGE entails both a considerable expansion of Norwegian biotechnology research and a nationally coordinated restructuring of the research establishment as a whole. The primary purpose of the plan is to guarantee that Norway stays abreast of international developments in research by strengthening ongoing efforts in functional genomics, integrating functional genomics into the focus of research activities in related fields, and building up the infrastructure needed both for these efforts and to increase national expertise in this sphere.

Currently, there are between 1 000 and 1 500 people in Norway working within areas in which functional genomics already plays, or will soon be expected to play, a crucial role. Of these, fewer than half have access to the equipment or know-how needed to conduct functional genomics research. Given the right conditions, many of these researchers would be able to incorporate functional genomics into at least some portion of their activities. This would help to restructure the research sector and generate new knowledge in a manner that is both necessary and desirable.

To ensure that Norway can compete with developments in other countries, annual government allocations of a minimum of NOK 300 million will be needed. Further, it is hoped that the private sector will increase its efforts and support to functional genomics as the universities, research institutions and other institutions of higher education enhance their level of expertise.

The objectives

FUGE has identified a number of objectives to be met within a framework of annual government allocations of NOK 300 million. These objectives are linked to the priority areas specified in Report to the Storting No. 39 (1998-99), *Forskning ved et tidsskille* (*Research at the beginning of a new era*).

Changes in the research establishment
FUGE will be an instrument for restructuring the Norwegian research establishment in order to ensure optimal results from allocations to research and to promote enhanced ties between the research community and trade and industry.

- Within one year, a system will be established to guarantee unified national thinking expressed through binding agreements for cooperation regarding

the distribution of responsibility for education, training and competence building.
- Within one year, regional and national networks will be set up to promote better utilization of costly equipment and investment-intensive infrastructure for functional genomics.
- Within two years, smoothly running national and regional cooperation schemes will be in place to integrate the research efforts within functional genomics carried out by trade and industry, the universities and the various research institutions.
- Within two years, contacts will be established with investor groups (and possibly with already existing enterprises) to promote commercial and industrial development.

Recruitment is essential

- At present, Norway does not have access to sufficient personnel to carry out the research needed within functional genomics. Recruitment is therefore considered a matter of priority. A number of researchers will need to be recruited internationally, and it will be particularly important to attract senior-level personnel (professors and post-doctorate researchers).
- Internationally, there will be a widespread lack of personnel with adequate qualifications in functional genomics, similar to that experienced within the ICT sector. Many of today's top researchers are seeking employment in countries such as Sweden, Finland and the USA, where there are excellent opportunities and conditions for research, and where substantial resources are being allocated.
- The regional centres must therefore be in a position to offer comparable terms (salaries and equipment) for research activities in order both to retain the qualified personnel currently working in Norway and to attract skilled personnel from abroad.

Basic biological research

FUGE is intended to bring the level of the basic research disciplines underlying functional genomics up to international standards. Furthermore, Norway will work to develop cutting-edge expertise in areas of particularly strategic importance, or in which the country has special advantages.

- Within one year, a scheme for researcher exchange programmes will be established to ensure that at least 70 per cent of the Norwegian fellowship students involved in these efforts will spend an extended period of their studies abroad.
- Within one year, a strategy to rapidly increase national know-how will be devised.
- Within two years, resource centres or networks encompassing all the key areas involved in functional genomics will be established.
- Within two years, key equipment and instruments will be renewed and brought up to international standards.
- In five years, the quality of Norwegian biosciences research is expected to show significant improvement.

Medical research

FUGE will help to make it possible for Norwegian health care services to utilize the new knowledge and medical products that result from functional genomics, thus ensuring that Norwegian health care remains on a par with top-quality services available elsewhere in the world.

- Within two years, Norway will have the expertise needed to utilize the material in biobanks in functional genomics.
- Within three years, functional genomics departments will be established at all national university hospitals, and these hospitals will be in possession of the knowledge required to utilize relevant new methods in the diagnosis and treatment of disease.
- Within three years, a system will be in place to ensure that all biological material stored in connection with health screening and surveys will be available for utilization in functional genomics research projects.
- Within three years, functional genomics methodology will be employed as the basis for studies of the impact of food on health, as well as for detecting foodborne pathogenic microorganisms and toxins.

Marine research
FUGE will play a role in establishing the research basis needed to promote further development of the aquaculture industry and optimal utilization of marine resources, as well as to establish a biomarine industrial cluster in Norway.

- Within two years, a network between the marine science research community and the marine-based industries will be established and in operation.
- Within three years, there will be a solid national foundation for research in bioprospecting.
- Within three years, Norway will assume a leading role in the understanding and utilization of commercially interesting aspects of the salmon genome.
- Within five years, there will be a solid national foundation for research in marine functional genomics directed towards mapping the genetic components for the growth rates, flavour, reproductive success and disease resistance of species of fish that are strategically important to Norway.
- Within five years, completely new, alternative systems for production of fish feed will be developed.

National distribution of responsibility

As functional genomics will play a key role in future biological research, it is desirable that basic know-how in this field be established in all the different regions in Norway. Since Norway has much ground to regain in relation to other countries, however, it is crucial to build competence in the major hubs as quickly as possible.

Norway does not possess the personnel, expertise or funding required to be able to “do everything everywhere”. It will thus be necessary to delegate responsibility to the various regions and among the various participating bodies within the regions. The individual research institutions must choose the areas on which they wish to focus, and national and regional priorities must be drawn up for the allocation of resources during the initial phases of the process.

Responsibility must be delegated on the principle that each research community or institution given primary responsibility for boosting know-how

within a given field, or for honing the skills needed to perform a demanding technique, is obligated to provide its services to the nation at large. High-cost equipment and expertise must be considered national property. Adequate travel funding must be made available to ensure that all groups involved may benefit from the national distribution of responsibility.

It is difficult to divide the tasks according to the priority areas contained in Report to the Storting No. 39 (1998-99), largely because these areas are so broad and overlap in so many ways. Tasks must therefore be assigned at a more detailed level, i.e. the various research groups must select specific aspects of the priority areas on which to concentrate their efforts.

Recommendations regarding future networks and infrastructure

Top-level international work in functional genomics requires both special technological know-how and costly equipment and instruments that depreciate quickly. These comprise the infrastructure that must be made available to the national research establishment.

Many of the techniques used in functional genomics will need to be available in all the various regions, although not necessarily to the same degree. Concentrated funding will be needed during a start-up phase to ensure that equipment and know-how are optimally utilized. This implies that certain institutions or regions will be charged with developing a high-tech service function for the rest of the country. For many such functions, it would be advisable to set up both regional and national networks within which the individual groups can exchange their specialized services.

The technology in this field is developing at an incredibly rapid pace. Equipment and know-how that are so complicated they are only understood by a select few specialists today, may be generally available and commonly utilized in the near future. For this reason, the delegation of responsibility and formation of networks must be viewed as a dynamic process. The infrastructure will have to change as the technology evolves. At the same time, it is important to think in a long-term perspective. Many of the technologies utilized in functional genomics require in-depth knowledge that takes time to acquire. The research groups assuming responsibility for such tasks must be guaranteed financing for the duration of the time it will take to acquire international-level know-how, and there must also be sufficient funding to ensure efficient operations.

The following list outlines some of the functional genomics infrastructure technology that will require the greatest amount of resources. The list also suggests a potential delegation of responsibility, based on what is known about the specific technologies today.

- DNA sequencing: This is the process by which the genome of a given plant or animal is described. Sequencers have been developed to conduct such analyses on the basis of very large throughput, but these are expensive and

depreciate quickly. An effort should be made to avoid investing in greater capacity than necessary. Sequencers that can conduct smaller-scale analyses are adequate for most research projects, cost less and are becoming standard equipment. High-throughput DNA sequencing is currently being carried out in Oslo and Bergen[2], and it would not be prudent to introduce these activities elsewhere. A better solution would be for Oslo and Bergen to assume responsibility for supplying these services at the national level. Smaller-scale DNA sequencing is being carried out within all four regions.

- Microarrays: This involves the production of DNA chips containing thousands of sample spots of immobilized genetic material that can bind to the specific genes of a target substance, after which the results are fed into a scanner and subjected to data analysis. To provide the genetic material for the sample spots, it must be determined whether clone banks (a collection of thousands of genes from the organism being studied) must be established. Trondheim, Oslo and Bergen will be responsible for developing the clone banks that are needed. These banks should complement one another in that each region should generate collections of genetic material from different species. A national network will be set up to ensure that the content of the clone banks is available throughout Norway. Responsibility for producing the DNA chips will be assigned to Trondheim and Oslo. Trondheim will establish a data warehouse in connection with microarray technology. These centres will be responsible for supplying the rest of the country with DNA chips and appurtenant expertise. All regions are expected to utilize this technology, which is a standard tool in functional genomics.

- Protein sequencing: This is the process by which the composition of various proteins is described. Protein sequencing has been carried out in Oslo for the past 30 years. National expertise in this area must be refined through the utilization of new technology, which will be introduced in one or more regions on the basis of closer consideration and national competition.

- NMR spectroscopy: The task here is to acquire the knowledge and equipment needed to produce images of proteins and genetic material in solution. The technology is found in all the regions, but needs to be upgraded and refined. Trondheim has been the site of a national centre for nuclear magnetic resonance for several years. This technology as such is standard equipment in most laboratories. Machines that can deal with the highest frequencies (over 800 MHz) are expensive, and should be reserved for one site on the basis of national competition.

- X-ray crystallography: The task here is to acquire the knowledge and equipment needed to determine the three-dimensional structure of proteins and genetic material in solid (crystallized) form. This service is already

[2] In the following, the terms Oslo, Bergen, Trondheim and Tromsø are used to refer to the regions to which these cities belong, and all the various institutions within that region.

available in Tromsø and Oslo, with Tromsø as the national resource centre. If there is a need for increased capacity, know-how about crystallization and the resolution of crystal structures should be developed in other regions.

- Other methods: Several other advanced technologies are needed to study proteins, especially the active portions of proteins, as well as other cellular molecules. Such technology includes special microscopy, optic and magnetic spectroscopy, and technology for large-scale proteome studies. Some of this will require substantial investment and special training. These services, although partially available at various places in the country, need to be expanded and further developed after closer consideration.

- Bioinformatics: The task here is to acquire the knowledge and equipment required to analyze the enormous volume of data needed in functional genomics both for statistical analysis and image processing. These services must be available in all four regions. The greatest challenge is recruiting personnel with sufficient IT expertise.

- Biobanks/health surveys: This involves making biological material and other information compiled from groups of humans, animals, plants or microorganisms available to researchers throughout the country. Trondheim has assumed the national responsibilities in connection with HUNT, the official health screening and survey unit in Northern Trøndelag county. Tromsø and Bergen have assumed similar responsibility for the health screening and survey units in Tromsø and Hordaland counties. Oslo is fulfilling the national responsibilities associated with an agricultural biobank. Corresponding national biobanks must be established for marine organisms. A national network for clinical biobanks must be further developed to ensure that the information stored in these is accessible for functional genomics research projects. One of the regions will be asked to serve as the hub for the network on the basis of an open competition. The task will be given to the institution/region that can demonstrate the best qualifications and greatest interest. It may prove useful to launch a company to deal with this task.

- Model organisms: This task involves establishing various model organisms to map the correlation between defined genetic modifications and changes in various traits in humans, animals, plants and microorganisms. A number of such models already exist (including yeast fungus, nematode worms, fruit flies, zebrafish, plants and mice). Model organisms are generally selected on the basis of the type of questions being asked. In a national perspective it is particularly important to find models that are relevant to research in the marine and medical sciences. Groups currently working with zebrafish in Bergen and Oslo must coordinate their activities. The introduction of transgenic mouse strains is a demanding, high-tech task. Consideration must be given to whether it is better to procure this service from specialized suppliers abroad or to produce such strains domestically. If it is decided to establish this function in Norway, it should be located in

Oslo. However, the work of breeding the established mouse strains will have to be carried out locally within each region.

Regional cooperation

FUGE will result in the establishment of a system for regional cooperation that integrates universities, research institutions and the commercial and industrial sector within subject areas that are relevant to functional genomics. Cooperation between these participants will be adapted to local needs, and will thus take different forms in the various regions.

In Oslo, an agreement of intent has already been drawn up outlining a strategic alliance between the University of Oslo, the Agricultural University of Norway, and the Norwegian School of Veterinary Science. The parties to the agreement are in the process of adding a number of binding measures to this agreement. It would be beneficial for this cooperation to be extended to other relevant research groups in the region as well.

In Bergen, the university has identified priority areas, or *Loci*, that will form the core of future regional collaboration. There is close cooperation between the University of Bergen, the Sars International Centre and the Institute of Marine Research, and the university will establish contact with the industrial sector in the region. It would be natural to include research institutions and industrial sector of the Stavanger area in these efforts. Together, these various players will constitute a western hub known as *"Biosentrum Vest"*.

In Tromsø a group has been established consisting of representatives of the university and the marine science research community. This group is expected to design the platform for future regional cooperation. Although industrial activity within this sphere remains relatively undeveloped in this part of the country, relevant companies will be invited to participate.

The University of Science and Technology in Trondheim has drawn up an individual strategy programme specifying the most important priority areas. Medical technology, in the broadest sense of the term, is one of the primary target areas. The region is already in the process of establishing wide-ranging cooperation in functional genomics with relevant players.

Cooperation with top researchers abroad

Two measures will be particularly crucial if the efforts to raise Norwegian research to international levels are to be successful. One is to encourage outstanding researchers from abroad, with broad-based international networks, to come and work in Norwegian laboratories and research institutions. The other is to allow Norwegian researchers to travel to other countries to learn from eminent research institutions there. By establishing ties between Norwegian researchers and top-level institutions in the USA, Britain, Germany and other leading research nations, Norway will gain access to the know-how it needs and, at the same time, raise the level of its national research efforts. Such contacts are also essential for boosting research-based industrial development.

In the short term, the goal is to enlist the support of the international research community in helping Norway keep pace with international developments. In the longer term, the goal is to make Norwegian research institutions so attractive to researchers and companies from abroad that Norway is considered an interesting partner in collaborative projects. Norway possesses a number of potential advantages that can facilitate this process, including biobanks linked to national health surveys and health-related registers for humans, farmed fish and domestic animals, as well as access to marine resources and undiscovered organisms.

Assessments of the Norwegian research community have repeatedly indicated that Norwegian research personnel are too tied to home; too few researchers have sought learning from research institutions in other countries. Thus, it is necessary to introduce special incentives. FUGE wishes to utilize expertise from abroad at three different levels, and will employ the following measures:

1) Individual cooperation (researcher to researcher) with top institutions abroad, particularly in the USA, but also with a number of European countries and Japan. FUGE will set up post-doctoral programmes that offer funding to personnel who wish to participate in research activities abroad. A career fellowship will also be introduced, initially providing the best researchers with financing for a minimum of 1-year's stay at a leading institution abroad, followed by a more substantial 3-5 year grant to build up corresponding activities at home in Norway.

2) Group or institution-based cooperation with the EU and international networks. FUGE will earmark special funding for the Norwegian research community to enhance necessary ties with other countries. A consultancy service for preparing applications will be created, and groups that choose to apply for EU funding will be rewarded in that those whose projects receive EU approval will be given priority during national allocation of funding. Efforts to promote greater participation in international researcher networks will also be intensified.

3) Institutional cooperation between the Nordic countries. FUGE intends to establish ties with MedCoast Scandinavia. Practical collaboration is already in place with the Wallenberg-Nord Consortium in Sweden regarding joint utilization of clone banks. The University of Oslo has initiated cooperation with Gothenburg University, and efforts will be made to establish broad-based contacts between various research institutions in Norway and the biotechnological hub emerging in the Øresund region. Similarly, it may be useful to promote cooperation with institutions in other Nordic countries, including Finland.

6 Translating plans into action

Budgets, organization and administration

Efforts to delegate responsibility and tasks in a national focus on functional genomics have already come quite far. The existing plan provides an excellent framework for these activities. However, there is still a need for a specific organization to deal with the follow-up and distribution of funding under FUGE.

Allocations of a minimum of NOK 300 million will be needed annually for five years, with an option to renew the programme for an addition five-year period if it has been successful. The funding could be distributed as follows:

1) infrastructure and networks: NOK 120 million annually,
2) support for projects and research groups: NOK 160 annually, and
3) regional efforts: NOK 20 million annually.

FUGE's organizational model should ensure excellent coordination at the national level with a strong base in the various regions. It would be useful to make use of advisory groups consisting of international experts, and clear lines of responsibility must be laid down in order to:

- ensure that the objectives of this national plan are met;
- ensure that joint services are maintained at satisfactory levels;
- follow up and analyze developments both regionally and nationally;
- promote cooperation and enhance the process of restructuring;
- evaluate applications from institutions, award grants and follow up progress reports;
- establish ties between university researchers, research institutions and trade and industry, thus laying the foundation for industrial development;
- promote and strengthen research administration at all levels.

Two categories of funding should be provided:

1) Large-scale grants to establish and operate joint services described in the section on distribution of tasks, e.g. grants for equipment with appurtenant personnel and know-how.
2) Funding for projects and research groups awarded in open competition, e.g. financing for larger projects and support for selected groups with a minimum amount of NOK 2 million per project/group.

Further details of the organizational model will be submitted at the latest by 1 May 2001.

If FUGE is to be successful, the Government must allocate a minimum of NOK 300 million annually over the next 5-10 years in addition to current allocations to biological research.

It is crucial that FUGE be viewed in conjunction with other government priority areas and policy instruments to exploit potential synergy wherever

possible. This applies particularly to the establishment of the Norwegian Center of Excellence, support for biotechnology-based industrial activity and other support measures from the Research Council of Norway. It will be absolutely essential to maintain a comprehensive approach if the research efforts are to be successfully translated into industrial growth. In keeping with this, the effort to develop suitable modes of interaction between FUGE and the industrial sector should be given top priority.