NATIONAL CONFERENCE ON AGRI-FOOD BIOTECHNOLOGY

Thursday, 1st June, 2000

Organised by:

Teagasc, NUI Galway, Trinity College Dublin,
University College Cork, University College Dublin,
BioResearch Ireland

Summary of Papers

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In 1999, the agri-food sector in Ireland accounted for almost 10% of GDP, almost 12% of employment and 30% of net export earnings. The industry is operating in a rapidly changing global environment and biotechnology is arguably the only technology that can seriously address the resulting challenges.

To maintain and increase our international competitiveness, Ireland needs to develop a serious biotechnology capability in the immediate future. To develop this capability, existing expertise and facilities must be harnessed into a multi-disciplinary and multi-institutional framework.

The emergence of modern biotechnology poses enormous challenges and opportunities for the Irish agri-food sector. There is a need to strike the correct balance between ensuring that we are at the forefront of emerging trends in the food industry in order to remain competitive, and exercising caution in further developing a new technology with an uncertain outcome. There is an obvious and urgent need to generate independent scientific data for the public on developments in biotechnology and their implications for the consumer, the environment and animal welfare. Such information will also improve our capacity to develop national policies on the issue and to contribute to decision making at EU level, where most of the key issues will be decided. Sound scientific research is a necessary base for informed discussion, regulation and exploitation of modern biotechnology.

There is a growing need for public research and development institutions to become more centrally involved in agri-food biotechnology. In the past, these institutions carried out credible, impartial research, which gave consumers the confidence in new and emerging technologies that are now commonplace in food production. Society must have trustworthy, credible and impartial evaluation and research to reassure consumers and producers of the benefits.

Scientific and technological excellence is necessary but not sufficient. It must be closely linked to a firm commitment to knowledge transfer and to convincing exploitation by industry and/or public interest organisations, leading to future wealth and job creation.

Underlying the proposed strategic research in plant biotechnology outlined in this paper is an effective plant breeding programme, operated by Teagasc, with commercial funding which has already shown itself well-placed to take up the results of basic science and incorporate them in successful new products. The end result of such work is an enhanced role for naturally-produced plant products in the diet of ruminants as well as an increase in the quality of the outputs; these advances can help increase both efficiency and quality, as well as facilitating traceability.

The Teagasc food research centres now meet the challenge of technology transfer through an innovation management strategy , the essence of which is the recognition that primary research information is not the end but the beginning of a process which continues until the usefulness of that information is established. For example, in Moorepark, the emphasis on innovation has yielded a number of patents and licences in biotechnology in recent years, demonstrating that a culture exists in the centre to exploit the outputs of a larger biotechnology programme.

Teagasc also benefits from the ability to combine production and processing research, allowing “farm to fork” type research to be undertaken. In this respect, enhancing our biotechnology programme will create a very powerful institute perfectly positioned to exploit discoveries generated through biotechnology. The very close links with our university colleagues also serve to strengthen that role.

The fundamental objective of today’s conference is to outline the priorities for an enhanced programme in agri-food biotechnology built around the existing university/Teagasc/BioResearch Ireland capability. Fundamental to this is the absolute requirement to obtain a significant level of funding from the Technology Foresight Fund. A new co-ordinated programme in agri-food biotechnology with a critical mass of skilled people, focused on key deliverable priorities, will generate new knowledge to fuel product development, strengthen the indigenous R&D base of this key industry and expand indigenous SMEs.

In pursuit of these goals, Teagasc's role is to be open, to present the results of research that is reputable and that has been subject to peer review, and to consider the range of options that are consistent with these results. To build and sustain public confidence, we need to address fully the genuine concerns of the users of technology and of the public, even when we do not share them. If we do not, then the consequences will be grave; initially for research, but ultimately for the potential beneficiaries.

Biotechnology Policy Framework
<u>The Universities' Perspective</u>

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The Technology Foresight Report sets a vision for a knowledge-driven Ireland and the Government has agreed to invest £560m over seven years in biotechnology and information and communication technologies (ICTs). The objective is to create highly visible, world-class research capabilities which will support the growth of knowledge intensive, high added-value industry in Ireland.

The universities welcome this very substantial investment in research and this presentation highlights their commitment to-date to achieving excellence in biotechnology and their willingness to play a key role in the implementation of the Technology Foresight proposals with particular relevance to applications in the agri-food sector.

It is accepted that biotechnology will be one of the core technologies of the 21st century with enormous potential for benefits related to agri-food, health, the environment and energy. The agri-food sector is the most important indigenous industry in Ireland, accounting for 30% of industrial output, exports valued at £5.5 billion and direct and indirect employment of 326,000 on farms, supply industries and ancillary services. As the sector faces challenges associated with competitiveness and globalisation, it is essential that advances in biotechnology research are harnessed across the whole food chain to facilitate consumer demands for high quality, safe, healthy foods that are produced in a sustainable environment.

The decision to invest in biotechnology research is especially timely in view of the ongoing successes in extending the frontiers of knowledge in a number of key relevant areas, such as the determination of whole genome sequence data for the human genome and those of plants, selected bacteria and yeasts; the molecular genetic basis for many disease conditions; the links between food and health and the development of animal and plant manipulatory technologies. The exploitation of this wealth of information requires the use of state-of-the-art facilities and expertise, particularly in proteomics and DNA array technologies, to demonstrate the function of key genes and to fully utilise biotechnology for the benefit of mankind in individual sectors such as agri-food and healthcare.

The universities in Ireland have long recognised the importance of biotechnology in their education and research programmes and are well positioned to participate in the Foresight Technology Programme based on:

- The world class achievements of several individual scientists and research groups
- The recent investment in biosciences within the Higher Education Authority Programme for Research in Third Level Institutions
- The diverse multidisciplinary research base available
- The favourable environment for the development of human capital provided by the combination of teaching and research
- The emphasis on collaboration and networking to enhance the research capability. Examples include: the Atlantic University Alliance; the Irish Universities Nutrition Alliance; the Dublin Molecular Medicine Centre and alliances with hospital research centres and the Teagasc Research Centres as well as international linkages
- The introduction of research management structures
- Successful technology transfer and commercialisation of research including the ability to spin-off new companies

With this background, the universities welcome the commitment to basic research in the Foresight Technology Initiative. Investment in people and equipment will permit world class researchers to achieve the scale and critical mass necessary to achieve their full potential and underpin the sustainable long-term development of the research system.

The biotechnology research programmes in the universities provide Ireland with the opportunity to take world leadership in the development of this technology and are directly relevant to the agri-food sector. In addition, the universities recognise the importance of strategic alliances with the Teagasc Research Centres to ensure that the benefits of biotechnology research targeted to priority areas within the animal, crop and food sectors are optimised. The programme should also address scientific issues that underpin the safety evaluation of novel processes and products and issues of trust and consumer responses to perceived risks. This strategy will help develop native entrepreneurship and will underpin the future competitiveness of indigenous and multinational agri-food companies in Ireland and help attract inward investment in areas such as functional foods and food ingredients.

Animal Biotechnology
Past, Present, And Future Possibilities

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In the broadest sense, biotechnology may be viewed as "The manipulation of natural entities for the direct benefit of humans or the benefit of systems upon which humans depend". With this view in mind, biotechnology is not new. Humans have practiced selective breeding programs in plants, microbes, and animals for centuries. What is new are the methods and views that comprise our efforts in biotechnology. Past selective animal breeding programs may be best exemplified by reference to dairy cattle. Since 1957, the average milk production for Holstein cows has risen over 124%. Although some of this increase must be attributed to improved management and nutrition, phenotypic selection for milk production has played a major role. However, selection for one phenotypic trait without an understanding of how this may affect other aspects of complex natural systems has led to several problems. Commensurate with an increase in milk production, inbreeding coefficients have risen dramatically, disease susceptibility has risen, and fertility has plummeted. Similar scenarios may be extracted in other animal systems.

A new age of biotechnology, based on genomics is at hand. **Genomics** refers to the study of an organism's whole genetic blueprint and the variations within that blueprint which make every individual in a population unique. **Functional genomics** seeks to relate differences in the genetic blueprint to physiology and phenotype. Although not mentioned specifically in other sections of this report, transgenics offer a powerful tool with which to study the function of genes once they have been uncovered. Several tenets of genomics are derived directly from our past experience in molecular biology. Perhaps the most important of these is that every nucleated cell in an individual carries the same genetic blueprint. It is the expression of particular genes at specific times in development that makes each cell perform its designated function. In other words, those genes that are actively transcribed into mRNA are responsible for the phenotype of a particular cell. It follows then that differences in gene expression or changes in the sequence of expressed genes is what gives rise to the various phenotypes in any animal population. New tools of functional genomics have been developed to visualize these changing patterns of gene expression in a more holistic fashion than was possible at any other time in biology. Functional genomics is also beginning to tie organisms and systems together, defining the basic underlying principles of life.

The Animal Functional Genomics Group at Michigan State University is working to discover new mechanisms related to growth and development in swine, immune competence and disease susceptibility in dairy cattle, and reproduction and fertility in dairy cattle. This diverse group of investigators has come together united through common threads that are defined by functional genomics. Strong institutional support in the form of other functional genomics programs, a central core facility, bioinformatics support, and an outstanding structural biology group have been key in the early success of this group. Setting aside individual egos and creating a "great group" mentality have also been key. Although each investigator maintains a strong independent research program, joint grant proposals, experiments, and publications are common. The impacts of functional genomics and other aspects of animal biotechnology may perhaps be best expounded through a review of programs currently underway within the Animal Functional Genomics Group.

The work of Dr. Catherine Ernst focuses on two important areas, genetic mapping and meat quality/muscle development in the pig. Creating the markers that will guide future generations of genomics researchers is an important aspect of Dr. Ernst's contribution to the group. Technologies such as chromosome painting, radiation hybrid mapping, and comparative mapping have been used to align regions of various swine chromosomes with counterparts in the human and mouse genomes. Because of these efforts, the wealth of information available from the human genome project can be used to define regions of swine chromosomes important in economic traits, such as meat quality, disease susceptibility, and growth. To investigate the differential regulation of gene expression during development, Dr. Ernst has used a technique called differential display reverse transcriptase polymerase chain reaction (DD RT-PCR). This technique offers a method of rapidly identifying many genes that are expressed in different amounts in two or more samples. To date, Dr. Ernst's group has identified over 15 genes that are expressed differently in fetal and post-natal pig muscle. Dr. Ernst's group has already mapped many of these genes to the swine genome.

Susceptibility of dairy cows to mastitis and other infectious diseases is highest during periods of stress, such as transport and calving. Dr. Jeanne Burton and the Immunogenetics Laboratory have focused on measures and causes of immune suppression during these periods. Of primary importance in fighting infections such as mastitis, neutrophils must migrate from the blood to the site of infection. Once there, neutrophils ingest bacteria and serve as the first line of immunological defense. It is neutrophils that make up the bulk of somatic cells in milk from mastitic cows. During periods of stress, neutrophil function is impaired and infections can become serious before the animal's immune system catches up. One of the primary impairments in neutrophil function during stressful periods is a reduced ability to migrate into infected tissues. During this time, neutrophils lose a cellular adhesion molecule known as CD62L or L-Selectin. Loss of L-Selectin prevents neutrophils from making solid contact with vascular walls and migrating into affected tissues. Dr. Burton's group has shown that synthetic derivatives of cortisol, which is released at high concentrations during the stress response, can similarly affect neutrophil function. The cortisol receptor is a protein that belongs to a class of molecules known as transcription factors. Transcription factors regulate gene expression either positively or negatively, depending upon the stimulus and cell environment. Dr. Burton's group has applied DD RT-PCR to demonstrate that, in addition to its effect on L-Selectin gene expression, the activated cortisol receptor may change expression patterns of many other genes important in immune function.

Not all animals (or humans) respond to stress in the same manner or are affected to the same degree. Ms. Jennifer Wells in the Immunogenetics Laboratory has uncovered a possible genetic reason for these differences. A major region of the cortisol receptor that makes contact with cellular machinery responsible for transcribing genes into mRNA is very different between individual animals as closely related as Holstein cattle. Using mass DNA sequence analysis and structural modeling, Ms. Wells has shown that these changes lead to a dramatically altered protein structure. Experiments designed to relate structural differences to functional changes are currently in progress.

In a related set of experiments, the Molecular Pathogenesis Laboratory has begun to look at a genetic basis for differences in susceptibility of cattle to Mycobacteria, including Johne's disease and bovine tuberculosis. The NRAMP gene has been shown to have a dramatic effect on survival of Mycobacteria in mice. In fact, a single amino acid change in the NRAMP protein is responsible for the BCG (Mycobacteria) resistant phenotype of some mouse strains. Recently, differences in the NRAMP gene region have been identified in cattle. We have begun mass sequencing of NRAMP protein coding regions from various cattle. In preparation for functional studies, the NRAMP gene is being knocked out in a continuous line of bovine macrophages. Macrophages are the natural host cell for intracellular bacteria such as those that cause Johne's disease and bovine tuberculosis. Divergent NRAMP coding sequences from cattle will be introduced into these macrophage cell lines and the resulting cells used to determine Mycobacterial susceptibility and survival. Our goal is to provide at least one genetic marker system that may be useful in predicting Mycobacterial susceptibility in cattle populations. This work has direct consequences for many other species, including humans.

The Animal Functional Genomics Group at Michigan State University has embraced a new way of looking at changing patterns of gene expression. DNA microarrays offer scientists the opportunity to examine changes in an unparalleled number of gene expression events in a single experiment. Using cDNA microarrays requires a significant investment in terms of both time and equipment to develop tools that will be applied to arrays. One such tool is an expressed sequence tag (EST) library for the species and tissues of interest. An EST library is essentially a collection of the gene segments that are expressed in a tissue or organism at a particular time and under a particular set of conditions. Using highly accurate robotics technology, segments of these ESTs are arrayed on specially prepared microscope slides. A standard microscope slide may hold as many as 2,000 to 3,000 EST segments. RNA from two different treatment groups is isolated and differentially labeled one with a green fluorescent dye and the other with a red dye, then hybridized to the arrayed ESTs. Special laser detectors are used to scan the array for fluorescence intensity. A computer combines the red and green images to form a composite image. Genes that are expressed the same in both treatment groups are displayed as yellow, those expressed in only one group are either green or red. In this manner, thousands of gene expression events may be visualized in a very short time period.

The impact of EST and microarray technology on domestic animal systems can be appreciated by examining the numbers of sequences currently submitted to public sequence databases, such as GenBank, over the past year. There are currently over

54,000 sequences from cattle in GenBank, with over 48,000 of these representing ESTs. In pigs, the numbers are smaller but similar in proportion. Significant numbers of EST sequences have not yet been submitted for sheep or horses.

The application of cDNA microarrays and EST libraries to programs within the Animal Functional Genomics Group will have a profound impact on the way in which we conduct experiments and on our science. We are convinced that complex traits, such as immune competence and muscle growth or meat quality, can only be understood through application of this type of holistic technology. The programs of Dr. George Smith and Dr. James Ireland also exemplify potential impacts of this technological revolution on animal science. Like Dr. Burton, Dr. Smith is also interested in stress and its effects on animals, including humans. However, Dr. Smith's focus is on how the brain regulates and controls the stress response, rather than on immunity directly. Dr. Smith has shown that corticotrophin releasing factor (CRF), which is released by the hypothalamus during periods of stress, acts directly on the pituitary to release additional factors that cause the adrenal gland to secrete cortisol. We have already discussed the profound effects of cortisol on immune competence. Controlling the release of cortisol through use of CRF antagonists (agents that prevent action of CRF) would be one way of controlling the effects of stress on animals and humans. Dr. Smith has shown that one such CRF antagonist is capable of reducing the severity of stress induced by endotoxic shock in dairy steers. Steers treated with the antagonist return to feed faster than control steers and do not suffer the affect of hyperglycemia characteristic of endotoxic shock. In the same experiment, Dr. Burton was also able to demonstrate a faster recovery in the immune systems of antagonist treated steers. A complex system such as the stress axis is best understood through use of technologies such as cDNA microarrays that allow correlations to be drawn from thousands of data points in a single experiment. To this end, tissues from endotoxin challenged steers have been collected and will serve as a source of mRNA for EST development.

Dr. James Ireland has benefited tremendously from collaboration with Drs. Boland and Roche at University College Dublin. This collaborative effort has spanned over 20 years and resulted in over 100 papers, abstracts, and presentations, not to mention many grants to support research on both sides. Dr. Ireland's research is focused on how development of ovarian follicles is regulated. One goal of this work is to design better methods to control fertility in dairy cattle. This research program has already contributed significantly to our understanding of factors controlling ovulation and folliculogenesis in cattle and humans. One practical application of Dr. Ireland's work is the immunization of animals against inhibin, a complex regulatory protein that limits ovulation rate or sperm output. Immunization of swine against inhibin resulted in over 200 more pigs from vaccinated groups than in untreated groups. A novel use of inhibin vaccines was found in dairy AI bulls, where immunization against inhibin resulted in a 45% increase in sperm output.

A new focus for the research programs of Dr. Ireland and Dr. Smith will be on maturation of oocytes and effects of aging on fertility. This new direction is a direct result of discussions within the Animal Functional Genomics Group and the advent of cDNA microarray technology. Drs. Ireland and Smith are currently collecting oocytes from cattle at various stages of growth for isolation of mRNA and EST development. Oocyte-specific cDNA microarrays will be used to address basic and practical questions in fertility and the effects of aging on expression of genes within the egg.

In summary, the age of Genomics is upon us and will have profound impacts on the ways in which we approach questions in the animal sciences. Embracing the technological developments that have led us to this point is a prerequisite for success. It is, however, not the technology that will drive the next great revolution in animal systems biology, it is the questions we will be able to address and the level from which we will have the privilege of looking. To those at ground level, there appears to be no order in the storm. It is only those who are able to view the system at a distance and see its entirety who see order among the chaos.

Biotechnology and the Precision Breeding of Forage Crops

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Within the UK, there is increasing interest in maximising the contribution of home-produced forage to the ruminant diet. Grazed forages are significantly cheaper than other food sources, and recent work in the USA has shown that they also have a beneficial effect on product quality.

The emphasis on breeding forages has shifted away from purely agronomic characters. Integration of work on rumen and silo microbiology and ruminant nutrition at IGER with the breeding effort has re-emphasised the importance of quality traits, both in terms of improving the efficiency of nutrition and the quality of the milk and meat that is produced. This emphasis on complex traits has provided further impetus for the IGER breeding programme to adopt biotechnological approaches.

The cornerstones of our breeding efforts in grasses, clovers and oats are:

1. The development of framework molecular maps
2. The mapping of quantitative trait loci onto these maps
3. The development of marker-assisted selection for these traits
4. The use of intra-specific and intra-generic hybrids to access a wider range of variability.

In the case of grasses, there is also a strong emphasis on physical mapping of traits onto chromosomes *via in-situ* hybridisation and the linking of this to introgression in order to generate hybrids that contain only desirable traits from the introgressed parent.

Transgenic technology plays a part in our breeding programme *via* feasibility studies, since it offers a rapid and precise approach to evaluating novel variation. Where targets show improved performance, we can use more conventional approaches to transfer the trait into an agriculturally viable background.

I shall illustrate these processes from our current breeding effort, emphasising our work on manipulating water-soluble carbohydrates in forage grasses and its link to improved animal production and increased nitrogen use efficiency.

Plant biotechnology priorities in Ireland

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1. Introduction

The agri-food industry in the next decade will operate in a rapidly changing world environment due to increased competitiveness, globalization of prices, and consumer demands for food quality, safety, health enhancement and convenience. It is therefore imperative to adopt new and innovative techniques to improve the competitiveness and efficiency of the crop sector. Innovation is essential for sustaining and enhancing crop productivity, and has always involved new, science-based products and processes which have in the past contributed reliable methods for increasing productivity and environmental sustainability. Irelands' capacity to compete will be dependent on the quality of our technology and the capacity of producers and processors to apply that technology. The set of techniques commonly referred to as biotechnology has introduced a new dimension to such technology.

Key core technologies will need to be developed to supply the appropriate crops and ultimately food products for an increasingly discerning and well-educated consumer. The benefits of biotechnology for the crops sector and consumers will be far-reaching. Biotechnology will bring cost savings to farmers by lowering their input costs to control insects and plant diseases. It will also help them obtain premiums for crops with improved traits. It offers the opportunity to minimise environmental risks by lowering the need for agricultural chemical applications and will be of benefit to the consumers by making future food products safer, more nutritious, longer lasting and less costly. In order to exploit the potential of this new technology for the crops sector in Ireland it is now imperative to initiate, conduct, monitor and harness appropriate developments in biotechnology in key strategic areas which will have most impact in the foreseeable future.

2. Key Research Areas

2.1. Genomics, proteomics and bioinformatics

The complexity of biological systems, coupled with the explosion in gene sequence information mandates the need for multidimensional methods for gene expression analysis. These are the key to "functional genomics", an area in which Irish research institutions/Universities must have strong capabilities to be competitive in the next 10-20 years. Plant genome scientists will increasingly employ DNA chips in research, and functional analysis of the genome through such approaches as gene knockout will be employed. Such tools are essential for genome researchers to move beyond sequencing and into the next phase of research where they conduct enormously large-scale gene discovery surveys and gene expression analyses.

Comparative genomics also provides information on allelic variation for genes controlling traits of agricultural importance. This will be important for structure-function studies as well as critical to understanding why one species or genotype performs better than another and hence is integral to molecular improvement strategies.

In the area of proteomics, the methods for analysis of protein profiles and cataloging protein-protein interactions on a genome-wide scale are technically more difficult but improving rapidly, especially for microbes. Functional genomics will impact most areas of biology, from fundamental biochemistry to improvement of quality and agronomic traits in crops, improved protection against pathogenic microbes, and improved exploitation of beneficial microbes.

The acquisition of relational databases, as well as the development of efficient methods for searching and viewing these data, constitutes a new discipline called "bioinformatics". Unquestionably, bioinformatics will be an essential component of all research activities utilizing structural and functional genomics approaches.

2.2. Gene Mapping and Marker Assisted Selection

Many important agronomic characters are controlled by genes which, individually have small effects (polygenes) and are untraceable by standard Mendelian segregation analysis. Quantitative genetics has been used to describe and analyse such genetic variation in terms of means, variance components, heritabilities, correlations etc. Thanks to the various genome mapping projects, many key agronomic plant genes can now be identified, as can genetic markers associated with important traits. This information makes it possible to use marker-assisted selection as a powerful new adjunct to traditional breeding methods. The availability of molecular markers has enabled detailed genetic maps to be produced for many species. By establishing linkage relationships between these molecular markers (tags), or preferably, for markers which flank the quantitative trait loci (QTL's) it is possible to use this information to enhance the efficiency of selection for those characters. Depending on the degree of linkage, these markers make it possible to trace QTL's in a breeding programme. This is what is meant by marker assisted selection (MAS). In addition these techniques will make it easier to identify populations which contain genes/gene sequences which compliment those in an existing breeding programme and make the selection of parents more precise so that favourable genes and gene combinations can be accumulated over recurrent cycles of selection. As this technique does not involve genetic modification it is not subject to the concerns associated with genetically modified organisms. Priority areas include:

Forage. Plant breeding programmes carried out by Teagasc, Oak Park is focussed on perennial ryegrass, white clover and potato. It is important that research on genome mapping and linkage analysis be carried out on these crops, so that new and improved varieties which are particularly suited to Ireland are developed.

Cereals. Cereals, mainly wheat and barley, constitute by far the largest section of arable crops in Ireland. Development of varieties with durable resistance to Septoria which is the major disease of wheat, the novel disease Ramularia in barley and barley-yellow-dwarf virus in both crops would reduce chemical usage considerably resulting in lower costs of production and much less risk of chemical residues in grain. This objective could be greatly enhanced through marker assisted selection in breeding.

Forestry. In forestry species quantitative traits, such as wood yield or wood quality can also be improved using molecular markers closely linked to, or located within, one or more QTL. The potential benefits of MAS are greatest for traits that are difficult, time-consuming or expensive to measure (for example, stem length/ girth and wood quality). Mapping and MAS may be justified for high-value hardwoods and have most potential when integrated with the development of selected varieties in an improvement programme, where additional genetic gains can be rapidly multiplied.

Nursery Stock. Nursery stock and ornamental plants are a growing sector of horticulture in Ireland. There is need to reduce imports and compete in the export market. Hence, the primary focus of biotechnology research in the horticulture sector will be generation and identification of new genotypes of ornamental plants and shrubs by using molecular markers, induced mutations and tissue culture.

Diagnostics. Molecular techniques such PCR, RFLP's, AFLP's will be used to detect the major crop pathogens such as fungi, bacteria, viruses and viroids. The technology will be used to research the epidemiology of new or emerging plant pathogens such as *Ramularia* and to quantify epidemiological or genetic changes in existing pathogens (e.g. *Phytophthora infestans*). Accurate identification of the presence of latent infection is critical for some disease control studies and can be an integral part of decision support systems.

2.3 Genetic Transformation

Genetic transformation of targeted crops (herbage, potatoes, cereals, hardwood trees and horticultural plants) may be desirable when useful genes, and the strategies for their utilisation are developed. It involves making particular constructs of the target gene, attaching it to an appropriate promoter, inserting it into the plant cells and regenerating whole plants from the transformed cells. There are many laboratories in Irish Universities and in Teagasc which already have a competence in the field of regenerating whole plants from cells and this competence can be used in the programme on genetic transformation of crops where required. Some university laboratories already have extensive experience in the production and characterisation of genetically engineered plants.

There are many genes / gene systems of interest, the following are examples:

- Tannin expression in white clover to prevent bloat.
- Barnase / Barstar male sterility system to facilitate hybrid seed production (target species, white clover, ryegrass)
- Biotic stress resistance (eg. oxalate oxidase to confer resistance to sclerotinia in white clover, resistance to Globodera pallidae and tuber moth in potatoes)
- Abiotic stress resistance (eg. low temperature, oxidative stress)
- Yield (eg. Manipulating scenescence and photoassimilate production and utilisation)
- Novel products (e,g. therapeutics/vaccines, nutraceuticals, novel oils, biopolymers)

The last of the above categories can be regarded as "Cell Factory" applications, in which the main limitation is often the amount of recombinant protein, or its products, produced. There is little doubt that one of the most important strategies here will be the transformation of chloroplasts, because of the spectacular amounts of recombinant protein which can be produced. In this arena, Irish laboratories are globally competitive, and constitute a rare research resource which must be nurtured.

2.4 Environmental safety of GMOs

Among the ecological issues associated with transgenic crops is the possibility that some newly introduced traits, such as pest or pathogen resistance, could confer added fitness to the crop. As a result, the crop may gain weedy characteristics if its ability to survive and spread outside of cultivation is enhanced. A second issue arises if such crops are grown in the vicinity of compatible wild or weedy related species; transfer of the trait by natural hybridization may produce hybrid progeny that are more aggressive or more difficult to control. These issues are no longer hypothetical, as at least seven groups of crops being engineered for pest resistance are known to have sexually compatible wild or weedy relatives. In many other countries, native weed relatives exist and transgene release is an issue. Rapeseed (canola) is an example.

Assessing the potential for transgenic pest resistant crops to become problem weeds, or to enhance the weediness of nearby sexually compatible relatives, is a complex task. Information is required from many disciplines e.g. weed science, agronomy, population biology and genetics, entomology, plant breeding, ecology, plant pathology, molecular biology, and more. Scientific evidence in support of informed risk assessment and decision-making thus lies in the collective knowledge of experts from these fields.

In this regard particular attention should be given to the following areas:

Background research and development is necessary to provide effective and acceptable procedures for testing and monitoring the relative impact of the products of plant biotechnology in non-target areas, so as to:

- develop inventories of pest infestations in related weed species
- determine the presence of pest resistance traits in weed populations
- quantify the impact of pests on weed populations dynamics in the absence of resistance
- create databases of sexually compatible species and varieties
- perform modelling studies to synthesise available knowledge and direct future research.

3 Targeted Research Areas

Approximately 90% of the agricultural land in Ireland is grassland and is the basis of a high proportion of the agricultural output now valued at over £3.5 billion. The most productive grasslands contain perennial ryegrass and white clover. The potential of genetics for herbage plant improvement can best be exploited through breeding which incorporates molecular biology techniques producing varieties which can fully exploit Ireland's climate advantages for grass production. Increasingly crops will have to be modified to suit the production environment rather than the other way round. Local adaptation will become more and more important in the varieties of the future and consequently it will be impossible to deny the need for local crop breeding programmes. The provision of varieties that are finely adapted to the "Irish production environment" should be a central theme.

In addition, traditional agronomic traits (eg. pest and disease resistance) as well as the development of biocontrol organisms for integrated pest and disease management which can be addressed through biotechnology, remain important targets for future improvement.
In forestry species quantitative traits, such as wood yield or wood quality can also be improved using molecular markers closely linked to, or located within, one or more QTL.

Nursery stock and ornamental plants are a growing sector of horticulture in Ireland, consequently, the primary focus of biotechnology research in this sector should be the generation and identification of new genotypes of ornamental plants and shrubs by using molecular markers, induced mutations and tissue culture.

Molecular techniques such PCR, RFLP's, AFLP's should be developed for the detection of major crop pathogens such as fungi, bacteria, viruses and viroids. Accurate identification of the presence of latent infection is critical for some disease control studies and can be an integral part of decision support systems.

In relation to genetically modified organisms, research should be aimed at addressing consumer fears, in this regard some important areas for research are:

- Environmental impact assessment of transgenic plants.
- Marker excision, and marker-free selection methods
- Improvements in gene targeting and transgene regulation
- Chloroplast transformation for biological containment and high level protein production (cell factory applications)

With the present controversy surrounding crops that have been modified for improved agronomic characteristics one of the purported reasons for the less than wholehearted acceptance by consumers is that the benefits are non-obvious to this constituency. The great hope for biotechnology in crop agriculture is the potential to use this technology to create crop products with obvious benefits to the consumer. Some of the potential target traits are as follows:

- Improved Shelf-life
- Nutrients (Nutraceuticals)
  - -- Macro: Protein, Carbohydrates, Oils/Fats
  - -- Micro: Vitamins, Minerals, Antioxidants, Isoflavonoids, Phytoestrogens, Condensed tannins
  - --Anti-nutritints: Phytase, Toxin and allergen removal
- Taste
- Novel Crop Products (eg. Oils, pharmaceuticals, vaccines)

Animal Biotechnology Priorities in Ireland

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Introduction

The revolution in biotechnology developments from the production of GM foods to the cloning of farm animals is brought to our attention almost daily. Biotechnology will make a highly significant contribution to Animal Production in future. It has been identified in the Technology Foresight report as one of the core technologies which Ireland must embrace. Biotechnology has developed at a rapid rate over the past 10 years and it is likely that it will continue during the next 10. It is an expensive science that must be treated both with enthusiasm and caution. The agri-food sector is operating in a rapidly changing world of increased competitiveness, increasing disposable incomes particularly in the developed world, and consumer demands for safer, better quality, more nutritious and convenient foods produced in an environmentally and animal welfare friendly way. This necessitates that food be produced in an antibiotic-free environment and thus there is a need to develop safer methods of producing the raw materials; diagnostic techniques that improve our ability to detect and prevent disease will be aided by developments in biotechnology. This paper indicates four main areas where biotechnology has the potential to benefit animal science in future.

1 Animal welfare
2 Disease management and prevention
3 Reproductive biotechnology
4 Genome analysis for animal improvement

Animal welfare

Animal production underpins much of Ireland's agri-food sector, in particular the dairy and beef sectors, the major component of the animal industry. Animal welfare, particularly in relation to high yielding dairy cows, pigs and poultry is a nationally important concern. Biotechnology, through the use of new diagnostic techniques for indicators of welfare will enable us to dramatically improve our ability to detect, and prevent problems relating to animal welfare.

Disease management and prevention

Infectious diseases have major implications for animal welfare and production efficiency, human health and food safety and quality. Mastitis in dairy cows is one such example that impinges directly on human health, as it influences milk quality. The emergence of antibiotic- and drug-resistant pathogens increases the risks for human health and poses a challenge for meat production, particularly since the recent withdrawal of feed additives which have helped to control disease to a relatively high degree. Biotechnology will enable the development of new and improved vaccines for disease prevention. Vaccines have the advantage that they are preventative, cost efficient, effective, and reduce or eliminate the need to use chemicals and antibiotics, thus minimizing the risk of resistance. Risks associated with DNA-based vaccines are less than those associated with conventional vaccines, which use all or part of the pathogenic organism.

Reproductive biotechnology

Reproduction efficiency underpins the major genetic gains that are being achieved in farm animals. Improvement in reproductive efficiency, in particular in high yielding dairy cows, is essential if the full genetic potential is to be exploited. Milk yield has increased significantly over the past 50 years, but this has been accompanied by a decrease in reproductive efficiency in the lactating dairy cow. Biotechnology offers a powerful tool to improve our understanding of the endocrine, physiological and genetic mechanisms involved in reproductive failure, particularly relating to early embryo survival. In the beef herd, the potential genetic gains possible have not been realized because of the difficulty of using AI as a result of poor expression and detection of oestrus in suckler cows. Biotechnology offers new approaches for the development of effective automated oestrous detection methods which can be applied in both dairy and beef cows. Gender determination is a major goal of the animal industry for many years. Separating sperm into X and Y fractions should dramatically improve efficiency of milk and meat production; current techniques are slow and invasive and the use of molecular biology for antibody detection may have important roles to play in sperm separation.

Genome analysis for animal improvement

Genome mapping for the farm species is making rapid progress, and complete sequences should be available within 5-10 years. Biotechnology is starting to provide an understanding of the mechanism of inheritance at the level of DNA. Most quantitative traits, such as growth are controlled by many hundreds of genes, each with a small effect. A gene with a large effect such as the halothane gene in pigs is the exception. The function of many of the genes so far detected is unknown. Nevertheless, the focus must be on identifying the key genes and other genetic and molecular markers associated with economically important traits, such as milk yield, meat quality and quantity, fat and protein synthesis in the mammary gland, disease resistance and ovulation rate in multiple ovulating species such as sheep and pigs.

There is a clear challenge to develop and exploit biotechnology to provide the technological advances necessary to underpin and sustain a competitive animal industry producing clean wholesome raw materials for the food industry. This will require a significant investment in research programmes that are multi-disciplinary and multi-institutional.

Food Biotechnology Priorities in Ireland

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The future international competitiveness of the food industry in Ireland will depend on its ability to innovate and diversify into new product lines/sectors in response to changing consumer and retailer preferences. An absolute requirement for such increase in sophistication in the industry will be the development of a national capability in food biotechnology which will enable the rapid high-tech expansion into value added novel foods and processes and away from much of the price supported commodities on which it now depends.

In this respect, the recent Foresight Technology Report stated that biotechnology will be ubiquitous in the agri-food industry in the early decades of the next millennium and proposed that significant investment be made in the area to increase the national capability in Biotechnology. In addition, the Report of the National Debate on Genetically Modified Organisms and the Environment states that "70% of the forecasted growth in biotechnology (in Europe) will be in the agri-food sector".

The report also commented that "in view of the importance of the agriculture and agri-food sectors to the Irish economy……(the) potential benefits could not be ignored". These comments are based on the realization of the enormous potential for improvement of food through Biotechnology in terms of yield, safety or nutritive quality.

In the food Industry, biotechnology has been exploited for millenia and well known examples include the selection of animal and plant strains for food production, the use of starters cultures to produce fermented dairy products and the use of yeast strains in the production of alcoholic beverages. Importantly, biotechnology embraces a wide range of technologies over and above genetic manipulation and includes fermentation technologies, protein separation technologies and the use of enzymes for food processing.

At present, considerable expertise in certain aspects of Food Biotechnology such as the genetic improvement of starter cultures which has been greatly facilitated through the Non-commissioned Food Research Programme funded by the Department of Agriculture, Food and Forestry has been developed in the country. Despite such advances, however, considerable "tooling up" will be required in order to achieve a level of biotechnological expertise in the country which can impact economically on our food products/exports. In particular, areas such as Food Safety and Nutrition deserve particular attention in response to a more discerning European consumer who has become increasingly aware of the impact of diet on health and wellbeing. Moreover, biotechnology has a lot to offer in these terms, be it through the improved rapid detection of food pathogens or the development of new ranges of Functional Foods with the potential to improve human health. In particular, the priority areas for biotechnology research in food include:

1. Food Safety:

Above all other attributes, the safety of food is an absolute priority, which must be assured in order to maintain or expand food markets. In this respect, there is an increasing need for increased food safety research, in response to global increases in food-borne disease allied to the exploitation of novel food processing approaches which could compromise food safety. Research will be necessary on the factors which effect pathogen performance in food systems with a view to introducing process controls which limit pathogen problems. The application of genetic technologies in food safety research offers greater sensitivity in the rapid detection of pathogens in food. Moreover, the genetic dissection of food-borne pathogenic bacteria using genomic and proteomic strategies will give an understanding into the mechanisms whereby these problematic organisms cause disease and how they manage to survive and/or grow in food systems and consequently how such problems may be avoided. The expanded National Research Programme should also include work on chemical contaminants, bio-protectants and food safety implications of genetically modified organisms.

2. Nuitrition and Health:

In response to the growing consumer awareness of the relationship between diet and health, there is also a need for increased research towards improving the nutritional status of many foods. Research is unveiling the existence within milk and meat of novel health promoting components, some of which are currently being exploited for the development of added-value 'Functional Food' ingredients or Neutraceutials, and is an area where biotechnology may provide potential new opportunities for the Food Industry. For example, the application of biotechnology to this area could allow the enrichment of foods with such components as vitamins, bioactive peptides and certain health-promoting fatty acids.

Probiotic Foods are currently the best known examples of Functional Foods in Europe, with health claims ranging from alleviation of symptoms of lactose intolerance, treatment of diarrhoea, cancer suppression and reduction of blood cholesterol. Dairy foods such as cheese and yoghurt provide the ideal food system for the delivery of these health-promoting bacteria to the human gut, however, research is needed both to improve the technological properties of these strains and to support the health claims associated with such products. In addition, the performance of probiotic bacteria in different food products needs to be studied with a view to diversification of the probiotic products available. Such foods may also have incorporated prebiotics which consist of fermentable sustrates which promote the proliferation of probiotic organisms in the intestine.

3. Food Quality and Flavour:

The quality of food rather than the price is becoming the dominant feature of competitiveness in food products' and ingredients' markets. In this respect, there are a number of examples where biotechnological approaches can be adopted to improve food quality such as the exploitation of novel starter cultures and starter adjuncts for flavour improvement in fermented foods. In this respect, the recent elucidation of the total genetic makeup of a cheese starter bacterium represents a significant milestone in our understanding of the cellular metabolism in lactococci, the most exploited food bacteria in existence.

Such detailed knowledge of the cellular mechanisms in these bacteria will be essential for the manipulation of starters, not just for the production of acid but as cellular factories; lactococci have been engineered to produce valuable metabolites including flavour compounds and some cultures have demonstrated the ability to produce health-promoting substances, such as the anti-carcinogenic fatty acid conjugated linoleic acid (CLA). Such advances have the potential to improve markedly both the health status and quality of cheese and may allow increased market access for dairy products into the health food sector.

Other opportunities of improving food quality emerge through the development of novel enzymes for meat and dairying applications and the use of molecular technologies to define the key determinants of product flavour and aroma. Indeed, the greater availability of new enzymes from novel sources will offer industry greater choices to innovate in food processing leading to the development of both a more diverse product range using more intense and novel flavour ingredients and the use of less severe processing technologies.

4. Selection of Animals for Food Production Based on Genetic Markers

The selective breeding of animals based on genetic markers for improved characteristics in meat and dairy processing holds tremendous promise for the future. For example, markers associated with such traits as meat tenderness, resistance to disease and improved milk processibility are currently being sought. With regard to the latter, it is already possible to select for animals that produce certain variants of casein which have an effect on cheese yield and functionality. In the future, it will be possible that the composition of milk will be controlled through the manipulation of the bovine genes governing the production of milk proteins resulting in 'designer milks' for particular applications such as milk with elevated casein content for cheese production.

In conclusion, the potential influence of Biotechnology on the food industry cannot be overemphasized and the future support a National programme in this area should undoubtedly lead to greater sophistication in industry with associated positive effects in terms of valus added products. As outlined above, Biotechnology should be seen as a horizontal activity across the industry which can positively impact on all sectors from the development of improved starter cultures for dairy fermentations to the genetic improvement of live stock for food production.

Biotechnology Research - Reaping the Economic Rewards

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The main focus of this conference is on the research priorities for Ireland in agri-food biotechnology over the coming decade, and the exciting research challenges that we face. However, as we embark on this new programme, I would like to discuss the importance of considering now the steps we must take to convert the technical advances that we are all confident of making,into economic benefits for Ireland.

Research activity influences economic development in many ways. The potential outputs include education of high-tech graduates; technical information of direct use to farmers, clinicians, industry and other researchers; as well as products and patentable technology. On top of which, a high quality national research activity will ultimately attract high-tech companies to locate in Ireland.

The government has accepted that there is a strong link between investment in the research and innovation base of the economy and sustained economic growth. In other words, the justification for the current investment in R&D is economic benefit. That is not to say that every basic R&D project funded is expected to show a specific commercial return. That would be neither appropriate nor feasible. However, there is clearly an expectation that the total investment will have such an effect. We in the Science and Technology community must meet this challenge, if we are to maintain, and indeed strengthen, the government's belief that this linkage exists.

In 1998, the Fraunhoffer Institute conducted a detailed survey of public investment in Biotechnology R&D in all member states for the European Commission. This showed that Ireland spent IR£7.22m per annum on biotech R&D and that BRI and Teagasc were major contributors to this total.

The good news for us is that at long last, the scale of the planned R&D investment will dwarf this spending, and about time too. The end result will be that many sectors of the economy should benefit from this increased investment.

Naturally, the current focus of attention is on the Foresight Fund, and on what research it should support, and on how it should be organised, assessed and run. However, if we are to ensure that we get a return on this investment, we need to build certain considerations into our planning from the outset. We need to consider the types of return we expect and require, and how we ensure that they are optimised.

The significance and magnitude of the current investment plan for R&D has changed everything, and we will need to rethink many aspects of our S&T infrastructure to take account of these changes.

Although the potential outputs are many, patent output is an easily measurable means of illustrating the need for planning. The experience of those countries that have made serious investments in R&D has been that it takes an R&D spend of a minimum of $1 million to produce 1 patent application. Of course there are no hard and fast rules, and once again I emphasise that this does not imply that Foresight should expect a patent in return for every million invested in a specific group. Ireland could theoretically expect some 200+ patents in the biotech field. Since each patent could cost up to £70K to submit and maintain, there are clear planning implications involved.

We must also remember that a patent is only the beginning. Moving a promising research discovery from lab to market is a complex, time-consuming and costly undertaking. Technology management is a multifaceted process, which requires attention by trained professionals if it is to succeed. In short, in addition to developing the infrastructure for research performance, we must also develop technology management structures and organisations if we are to ensure that the outputs of our R&D efforts are made available to users.

Ireland's S&T infrastructure is highly dependent on universities and other Higher Education colleges as research performers. This has many advantages. The US experience of university research is certainly encouraging. A recent study showed that in 1988 US university technologies resulted in the establishment of 364 new companies; 385 new products and 3668 licences. However, US colleges have well-staffed Technology Transfer offices whose function is to ensure the transfer of research results to external users.

At the moment Ireland has a technology management infrastructure developed to cater for a low R&D investment economy. There are less than 30 staff involved in managing the transfer of technology from our research performers (i.e. universities, Teagasc etc). Any one of the larger US universities would have a similar number of technology transfer staff. Our technology management infrastructure will therefore require a significant boost in financial resources if it is to be capable of managing the increases in activity that we can anticipate.

It is not the process of discovery, but putting new knowledge to work that creates market value. If managed properly, such knowledge can fuel innovation in the marketplace, and add value to our agri-industry. This will contribute to the growth and development of our agri-food sector and the welfare of consumers. The immediate users of the results and technologies emerging from R&D are; farmers & growers, existing food industry, agribusiness companies, new start-up companies. These will be the targets for our future technology transfer activities.

As a major organisation involved in commercialising university R&D, BioResearch Ireland's function has been to play a leading role in both transferring technology and fostering the creation of new companies. Since 1990 BRI has invested a total of £22.64m in university R&D, resulting in 5 spin-off companies, 33 patent submissions, 10 granted patents and 5 licenses world-wide. By any standards BioResearch Ireland has been very productive in commercialising biotechnology research.

BioResearch Ireland looks forward to significantly increasing this activity to the benefit of all.