DOUGLAS ORMONDE BUTLER MEMORIAL LECTURE

NEW ANIMAL GENETIC TECHNOLOGIES - GOOD OR BAD?

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INTRODUCTION

Over the next decade, animal breeders will be increasingly confronted with a range of new animal genetic technologies. The technologies will be based upon the outputs from genome mapping and gene transfer research and are being developed from a genetic information database which is expanding rapidly. Hence, the power and impact of the new technologies should increase substantially over time.

The new technologies promise to dramatically change the way livestock are bred for the production of meat, milk, fibre, eggs and leather as well as byproducts. In particular, the rate at which new genetic lines of animals can be bred to produce new or modified products will be accelerated. Such technologies will be important because rapid responses will be necessary in order for the livestock industries to maintain their competitive position in the face of increasingly discerning, fickle and safety conscious consumers.

In this presentation, I will briefly describe the genetic revolution which is underway and then review the current status and future prospects of the new technologies which are emerging. Finally, a number of issues related to the social implications, long term sustainability and ethics of the new technologies will be discussed. Given the substantial benefits expected from the new genetic technologies, it is likely that the industry will adopt them in some way. However, the form of the new technologies must have input from all stakeholders including end users, service providers, scientists and the general public.

THE GENETIC REVOLUTION

Although the basic laws of inheritance were well known from Gregor Mendel's studies over 150 years ago, the precise makeup of genes remained a mystery until the discovery of the chemical structure of DNA by Watson and Crick in 1953. The mammalian genome comprises approximately 75,000 genes spread over chromosomes within the nucleus of cells. Physical size has been estimated at 3 x 10^9 bases (3000Mb). Phenotypes or traits measured/observed on an individual may be determined by a single gene (ie monogenic), or more commonly, by multiple genes (ie polygenic). In each case, environmental factors may also influence the phenotype. For these reasons, most phenotypes display continuous variation over a broad range. Determining the molecular genetic basis of such traits is not a trivial task but is being facilitated by ongoing technical advances.

Current status

Genome research around the world was given a significant boost when the US government initiated the Human Genome Project (HGP) in 1990. The project, now supplemented by similar projects in most western countries, has the ambitious goal to map and sequence the entire human genome within 15 years. In the course of the project, many tools for genetic analysis, technological breakthroughs and research infrastructure are benefiting genome research on other organisms such as livestock. As part of the HGP, genomes of model organisms such as the bacterium *Escherichia coli,* yeast *Saccharomyces cerevisiae,* roundworm *Caenorhabditis elegans,* fruit *fly Drosophila melanogaster* and the laboratory mouse *Mus musculus* are being characterised.

Progress to date has been impressive. Framework human genetic and physical maps are complete with more detailed maps under construction. Partial DNA sequence for many of the estimated 75,000 human genes has been obtained and mapping of the genes is underway. Large scale sequencing of some human chromosomes has recently been initiated with some observers suggesting the task of sequencing the entire human genome may be completed several years ahead of schedule.

Progress with model organisms has been no less spectacular. The genome of *S.cerevisiae,* comprising 15 million base pairs (15Mb) has been completely sequenced, as have the genomes of *Haemophilus influenzae* (1.8Mb) and *Mycoplasma genitalium* (0.58Mb). Framework genetic and physical maps of the

mouse are also well advanced.

DNA sequence databases are growing at an astounding rate. Genome databases, comprising information on the location of genes as well as genetic and physical markers, are also expanding rapidly. At this point in time, slightly more than 5% of all human genes have been isolated and mapped. For other organisms, the numbers are lower. However, the situation is changing rapidly, with a full catalogue of all 75,000 human genes likely to be available (with partial sequence data) within five years.

Expanding the genetic database

Genetic knowledge is being expanded at a number of levels, viz. DNA sequence data, isolation and mapping of genes, assigning functions to genes and finally associating genes with phenotypes. At the present time, sequencing of whole genomes is being undertaken only with organisms of relatively small genome size. The *C. elegans* (100 Mb) and the *E. coli (4* Mb) genomes are expected to be completely sequenced by 1998, while 2.5 Mb of sequence has been obtained for *D. melanogaster*. Several human chromosomes are being sequenced as pilot projects for the main sequencing project to follow. Sequencing of newly isolated genes is also occurring on a wide front. Consequently, sequence entries into the Genbank sequence database have increased five fold since 1990 and are still increasing exponentially.

Over the past three years, a number of privately and publicly funded projects have set out to obtain partial sequence data (EST) for all of the genes expressed in human and mouse tissues at different developmental stages. The task is nearly complete for human. Predictably, only a small proportion (eg less than one third) of these genes match up to previously characterised genes. Predictions of likely functions are possible for less than half of genes sequenced, but for the remainder, the task lies ahead. Progressively, genes in the catalogue are being mapped on the genome for subsequent use in positional isolation studies.

Livestock activities

Livestock genome research has gathered pace during the past decade (Hetzel 1993). Genome projects, many based on international collaboration, are underway for most of the agriculturally important animal species. However, R&D activity is several orders of magnitude lower than in the "master" mammals (ie human, and the mouse).

Fortunately, information on the gene sequence in one organism can be used to rapidly isolate the gene homologue in even distantly related organisms. The function of genes is widely conserved especially across mammals. As well, the conservation of blocks of genes through the process of evolution, means that approximate gene location can be predicted from comparative maps (O'Brien *et al.* 1994). Thus, livestock genome researchers can utilise much of the genetic information which is being generated as part of other genome projects in addition to the information on their own species. This information will be the raw material for the development of new animal genetic technologies.

EMERGING ANIMAL GENETIC TECHNOLOGIES

Three technology areas will be discussed, ie genotype based selection which is becoming feasible because of the development of genetic tests for production traits.; gene transfer which is becoming an increasingly powerful technique for making transgenic livestock; accelerated breeding programmes which combine genetic technologies with rapid generation turnover and multiplication technologies and hold much promise.

Genotype based selection

Genotype based selection makes use of genetic tests for production traits. These tests are based on gene variants which have been associated with individual differences in phenotype (eg morphology, anatomy, behaviour or productivity). The test may detect the gene variants directly or through genetic markers which are known to tag the gene variants.

The Research Task Research is required to define which gene variants or markers are associated with which traits and in which breeds, herds or flocks the associations apply. Associating a gene to a particular phenotype is also an important step in assigning functions to genes. Whilst it can be a relatively straight forward procedure if the gene product (protein) is known, this is an uncommon situation, especially with complex phenotypes. In such cases, the first step is to determine which gene or genes are responsible for the variation in a phenotype.

There are two general approaches to mapping and isolating genes for which the gene product is unknown. The first of these, referred to as the candidate gene approach, relies on some background biochemical knowledge and is therefore limited in its application. However it must be appreciated that an altered level of a particular enzyme or other gene product does not imply an alteration in the structural gene for that product. Gene expression is frequently very complex, involving a number of regulatory genes, in some cases located at distant parts of the genome. Nevertheless, an hypothesis of whether variability exists at or around the site of a gene can be tested wherever appropriate reagents and pedigrees are available. The requirements include multigeneration pedigrees with appropriate phenotype data. The optimum pedigree structures will differ depending on whether simple or polygenic inheritance is expected. There is a requirement to measure genetic variability at the candidate gene locus. DNA markers are most frequently used for this purpose. By analysing for co-segregation at the candidate gene locus and locus of interest, the hypothesis of association can be tested.

The second approach to isolating genes utilises a positional strategy by initially localising a gene to a chromosomal segment generally via anonymous genetic markers (Figure 1). The markers will be chosen from a genetic map to ensure complete screening of the genome with a minimum number of markers. Assuming there are sufficient informative meioses to be analysed, linkage between one or more of the mapped markers and the gene or associate phenotypic effect will be found. Detailed analysis of the segment can refine the localisation and lead to isolation. The positional approach is inherently more laborious, but has a higher probability of success and requires no knowledge of the function. It is equally applicable to simply inherited and polygenic effects although the optimum pedigree structures will vary and there is a limit to the size of gene effects detectable in the polygenic situation.

The two approaches are not mutually exclusive. Once the search for a gene is narrowed down to a discrete region, genes previously mapped to the region may suggest themselves as candidates. In addition, homologous regions in other genomes can also be surveyed, thereby expanding the number of potential candidates. So in practice, a combination of both approaches is appropriate, especially as mammalian gene maps become denser, providing a larger number of potential candidates.

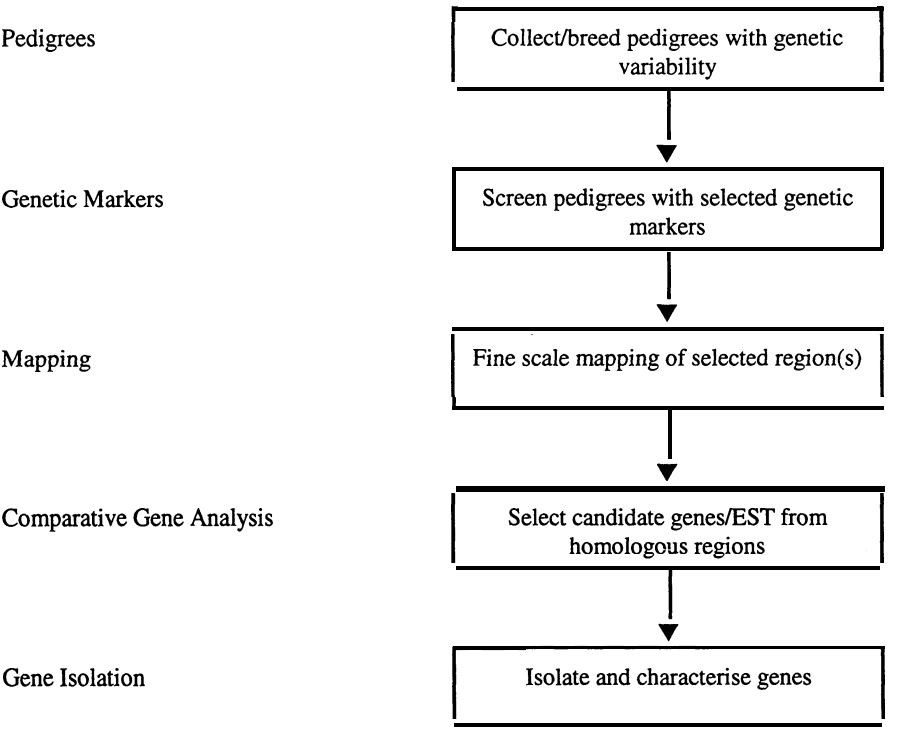

Figure 1. A positional strategy for isolating a gene

Current status of genetic tests Genetic tests are being developed for a range of traits in livestock. Some of the tests which are currently commercially available are listed in Table 1. For obvious reasons, the monogenic traits such as genetic disorders and morphological traits have been more amenable to analysis. However, genes affecting polygenic traits are now being identified and genetic tests are being developed.

Genetic disorders, due to a single gene defect, are relatively uncommon in livestock because affected animals are usually disposed of. However, in higher value livestock such as cattle, such disorders may persist in the population. The Holstein-Friesian dairy breed carries the most disorders because artificial breeding is common, leading to higher levels of inbreeding. In almost all known cases of disorders, a single point mutation is responsible. Furthermore, the disorders tend to be breed specific.

Amongst the morphological traits, coat colour is important in many livestock. In pigs, the dominant white condition has been found to be due to a duplication of all or part of the KIT gene and is now being used to breed white crossbred pigs. A point mutation in the melanocyte stimulating hormone receptor (MSHr) gene affects the relative amount of eumelanin and phaomelanin pigments in cattle and thus the intensity of pigmentation. The poll gene has not yet been isolated in either cattle or sheep although close flanking markers are known. In all the above instances except the poll gene, similar conditions in mouse and human have provided useful starting points from which to isolate the gene in animals, thus emphasising the importance of the genetic information database in other organisms (Table 1). Some genetic tests which are commercially available for livestock.

Table 1. Some genetic tests which are commercially available for livestock

Test	Gene	Species	Reference
Genetic disorders			
Bovine leucocyte adhesion deficiency (BLAD)	CD18	Cattle	Shuster *et al.* (1992)
Pompe's disease	GAA	Cattle	Reichmann *et al.* (1994)
Uridine monophosphate synthase deficiency (DUMPS)	UMPS	Cattle	Schwenger *et al.* (1993)
Weaver disease	Chrom. 4 markers	Cattle	Georges *et al.* (1993a)
Morphological traits			
Dominant White coat colour	KIT	Pigs	Moller (1995)
Red/Black coat colour	MSH-R	Cattle	Klungland *et al.* (1995)
Poll[A]	Chrom. 1 markers	Cattle	Georges *et al.* (1993b)
Production traits			
Porcine Stress Syndrome/Halothane sensitivity	RYR	Pigs	Fuji *et al.* (1991)
Litter size	ESR	Pigs	Rothschild *et al.* (1994)
	FECB	Sheep	Montgomery *et al.* (1993)
κ casein	CSN3	Cattle	Schlieben *et al.* (1991)

[A] Evaluation studies in progress

Several major genes have been mapped for production traits, and diagnostic tests are available. The porcine stress syndrome (PSS) test has been widely used in the pig industry to remove susceptible and carrier animals. Variants of the oestrogen receptor (ESR) gene are associated with effects of nearly 1.5 piglets per litter. Although the Booroola prolificacy gene (FECB) was mapped several years ago, and close flanking markers have now been identified, the gene is yet to be isolated.

Several other major genes affecting muscle growth have recently been reported. A gene causing muscular hypertrophy (CLPG) in Dorset sheep has been mapped to chromosome 18 and isolation studies are underway (Cockett *et al.* 1994). Unfortunately, whilst the gene causes increases in muscling (32%)

and decreased fat content (8%), there appears to be reduced muscle tenderness under some circumstances. The mode of inheritance is also unusual in that the gene is expressed in the heterozygous state only when inherited from the sire.

The gene responsible for double muscling(MH) in Belgium Blue cattle has recently been mapped to chromosome 2 (Charlier *et al.* 1996). Homozygous animals are difficult to maintain since they must be born using cesarean section due to their increased birth weight. However, heterozygous animals have superior meat quality, ie reduced fat and connective tissue. It will be interesting to see whether other variants of the gene, perhaps with reduced effects on pre and post natal growth, exist in other breeds.

Genes with smaller effects than, for example, CLPG and MH have been more difficult to identify, but are likely to be responsible for most of the individual animal differences in commercially important traits. Such genes, termed quantitative trait loci (QTL), have been until recently more difficult to map and isolate with the techniques available. Nevertheless, in the last few years it has become feasible to investigate such genes and QTL studies are now underway in beef and dairy cattle, pigs, sheep, chickens and dogs.

The first step in QTL studies is to identify the chromosome regions where the QTL reside (Figure 1). Published results from two studies completed to date are encouraging. Georges *et al.* (1995) reported chromosome regions with large and significant effects on milk yield, protein and fat content in dairy cattle, whilst Andersson *et al.* (1994) found QTLs with significant effects on growth, backfat and intestine length in pigs. In a study carried out under the CRC for Meat Quality, chromosome regions with significant effects on growth, tenderness and lean meat yield in beef cattle have also been identified.

It is expected that QTL studies will identify chromosome regions containing genes which affect a wide range of traits, although it will be some time before the gene variants responsible for the phenotypic differences will be isolated. In the meantime, it will be necessary to use genetic markers tagging the genes in breeding programmes. Such methodologies are constantly being refined but require caution in their implementation (Kinghorn *et al.* 1994).

Genotype based selection in practice

Genetic tests reveal the underlying genetic makeup of an individual for a particular gene. For monogenic traits ie determined by a single gene, such tests are highly accurate whether based on the gene variants themselves or on closely linked markers. But for polygenic traits, accuracy will depend on how many of the major genes (QTL) have been identified.

Genotype based selection will have most benefit for traits which are difficult or inefficient to select for using performance recording schemes. Such situations include sex limited traits (eg milk production), traits measured late in life (eg eye cancer), traits which require sacrifice (eg carcass and meat quality), traits which are difficult to measure (eg disease resistance), and low heritability traits such as reproduction.

For polygenic traits, it is likely genetic tests for QTL will be combined with information from performance recording and progeny testing programmes in order to maximise the accuracy of selection. A variety of schemes are optimal, depending on whether the genetic tests are based on the gene variants or linked markers (Kinghorn *et al.* 1994).

Transgenic livestock

Transgenic livestock carry additional genes introduced by gene transfer techniques. Gene transfer can be used to introduce new or modified genes into the germ line of animals such that the gene is inherited together with the rest of the genetic material. Pioneering work in mice by Palmiter *et al.* (1982) heralded a number of attempts to produce transgenic livestock with improved phenotypes. In the ensuing 14 years, transgenic pigs, sheep, cattle, rabbits and chickens have been produced. However, numbers have been small and significant difficulties have been encountered. To date none of the transgenic animals, with the exception of those developed for the production of specialised pharmaceuticals, have proved to be commercially viable. Microinjection techniques have proved to be of low efficiency in livestock, producing less than 1% transgenic offspring per embryo injected (Rexroad 1992). Cheaper systems of embryo production as well as methods to select for viable embryos are required.

Part of the problem with the expression of transgenes may relate to the so called position effect, ie where the regulation/expression of a gene is influenced by adjacent sequences/genes. In mice, targeted insertion via homologous recombination is achieved through the use of embryonic stem cell lines. Cells isolated from the inner cell mass of blastocycst stage embryos can be cultured *in vitro* under specific

conditions. Such cells retain their totipotency, ie ability to subsequently differentiate. Site directed gene insertion can be achieved *in vitro* using homologous recombination, and appropriately modified cells can be injected into the blastocoel cavity of a host embryo. To date true embryonic stem cells have not been produced for organisms other than mice although a recent study in sheep is encouraging (Campbell *et al.* 1996). If cell lines can be readily established, some of the technical problems associated with producing transgenic livestock will be solved.

Manipulating growth Early transgenic studies focused on incorporating additional copies of the growth hormone gene, sometimes with spectacular results. For example, Purse1 *et al.* (1989) reported elevated levels of growth hormone, improved growth, feed efficiency and reduced fatness in transgenic pigs. However, associated effects included ulcers, arthritis and joint problems. Other groups tried using a variety of promoters as well as growth hormone genes from different source species with variable but generally disappointing results (Rexroad 1992). Failure to achieve tight regulation of the promoter generally had pathological consequences. Manipulation of growth by gene transfer has now been abandoned by most research groups.

Novel *biochemical pathways* Gene transfer offers the means to introduce novel biochemical pathways into livestock. In Australia, significant efforts over the past decade have focused on improving wool growth by introducing the genes required for cysteine biosynthesis into sheep (Rogers *et al.* 1995; Ward *et al.* 1995). However, to date expression of the introduced genes in the wool follicle of sheep at sufficiently high levels and in concert with other genes has not been achieved. Attempts to use the plant derived chitinase gene to inhibit insect pathogens are also being investigated (Ward *et al.* 1.995).

Modification of milk One apparently successful application of gene transfer in livestock is the use of transgenic animals to produce valuable proteins in their milk. To date, high level expression of alpha 1 antitrypsin in sheep (Wright *et al.* 1991) and human haemoglobin in pigs (Sharma *et al.* 1994) has been achieved. A feature of this use of transgenic animals is that only small numbers of animals are required to meet the world's demand for the high value human pharmaceuticals. Further products of the type can be expected from the technology in the future.

Overall, whilst the production to date of commercially useful transgenic livestock has been disappointingly low, future prospects appear bright. Genome projects are providing a rich selection of genes which may be suitable candidates for gene transfer. Our knowledge base of the complex hierachical regulation of genes is also improving which will in turn lead to the identification of suitable processes to target. Thus, as gene transfer techniques are refined over the coming decade, transgenic livestock could be increasingly used in commercial production.

Accelerated breeding programmes

The full power of new genetic technologies will be realised when used in combination with reproductive technologies which reduce generation time and enable large scale multiplication of genetically superior lines. The objectives and outcomes of animal breeding programmes are new lines of animals which suit a particular market niche and production system. Genotype based selection and/or gene transfer are tools the breeders can use to package the desired sets of genes. Advanced reproductive technologies will speed up the production and distribution phases of breeding programmes and thereby provide an earlier and potentially greater return on the breeder's investment.

Reduced generation interval *In vitro* embryo production techniques now allow the collection of large number of oocytes from hormonally stimulated females. Techniques for the *in vitro* maturation and fertilisation of the oocytes, and subsequent embryo maturation are being refined. For example, Earle *et al.* (1994) reported that ovaries of six week old ewes could be stimulated to produce an average of 60 oocytes and 15-20 blastocysts. Similar results have been reported for cattle (Armstrong *et al.* 1992). Although live lambs and calves have been produced using these methods, pregnancy rates have often been low. Nevertheless, since oocytes can be collected regularly from juvenile females, annual embryo production rates are potentially high.

The long generation intervals in cattle and to a lesser extent in other livestock are a major impediment to genetic change. Rarely does a line of animals have all the desirable genetic attributes. Short generation turnover breeding schemes will expedite breeding programmes, as long as animals can be screened at a young age for the desired genes/characteristics. Genotype based selection, particularly when applied at the embryo level and used with pedigree performance data, will make such programmes feasible.

Where a particularly valuable gene(s) is present in an unproductive genetic background (eg disease resistance in an unimproved breed), an introgression programme to breed in the gene(s) into a productive breed may be appropriate. Georges and Massey (1991) proposed that rapid introgression using genotype based selection on *in vitro* embryos produced from foetal oocytes could achieve two to three generations per year. Whether or not such a scheme is ever used in practice remains to be seen. However, it is clear that rapid generation turnover when used in combination with genotype based selection either on embryos or at the juvenile stage is a very powerful combination.

Rapid multiplication There are two promising avenues for dramatically increasing reproductive rate in ruminants. The first of these involves the collection of preantral (immature) follicles from the ovaries of females. Several thousand of these follicles are produced during an animal's lifetime. Recent research indicates that the follicles can be collected without the need for hormonal stimulation, and matured *in vitro* (Figueiredo *et al.* 1993). Although a number of technical obstacles remain, such a procedure would significantly reduce the gap between male and female reproductive rate and accelerate breeding programmes.

A second approach, known as cloning or clonal propagation, has been on the threshold of practical reality for a number of years. A recent study in sheep was apparently successful (Campbell *et al.* 1996). With this procedure, genetically identical copies of an embryo (not an animal!) are produced by placing undifferentiated cells from a developing blastocyst or embryonic cell line into enucleated oocytes. By repeating the procedure once the new embryos reach blastocyst stage, a potentially large number of identical embryos can be produced. To date, clone families of up to ten have been reported. However, there has been a common problem with 'large foetus syndrome', whereby a proportion of embryos develop into exceptionally large foetuses, raising veterinary and welfare issues.

Assuming that large viable clone families can be produced in the future, genetically superior lines once produced could be rapidly multiplied. For example, a number of clone families could be produced for each line and stored as embryos. A small number of each family could then be reared and evaluated for performance. Other members of each family (ie still as embryos) could then be sold with guaranteed performance for a particular production system since they are genetically identical to the clone family members which were evaluated. Thus cloning will be an extremely useful tool for the production of commercial stock, once a genetically superior line is established.

WIDER IMPLICATIONS OF THE NEW TECHNOLOGIES

Before wholesale adoption of any new technologies, it is prudent to consider the wider implications of industry implementation. The new genetic technologies, particularly when combined with advanced reproductive techniques, could result in a number of significant changes to the structure of our livestock industries. In the first instance, greater intensification of production will probably occur in order to increase throughput. Continuing economies of scale will also result in production units becoming larger. Such changes have already occurred with the pig and poultry industries. Secondly, the general pace of technological change will increase and enterprises will need to adopt new technology at a more rapid rate to remain competitive, ie 'tech up' or 'ship out'. In particular, if the new genetic technologies are as beneficial as predicted, breeders relying on traditional technologies will find it difficult to compete. Thirdly, greater integration of breeding, production, processing and marketing will be inevitable. Integration is not a novel concept in agriculture but until now it has not been widely adopted in the cattle and sheep industries. Integrated enterprises benefit from more effective consumer feedback and the accumulation of productivity gains at each step of the production and marketing process.

None of the above predicted structural changes will be solely attributable to the new genetic technologies. However, the availability of more productive lines/strains of livestock will drive the change towards more economically efficient production systems. A number of social, scientific and ethical issues will need to be considered.

Social effects

A move towards fewer larger specialised breeding units will result in reduced labour requirements. Throughout history, adoption of technology has usually caused a drop in labour demand. However, for Australia, one of the most urbanised countries in the world, the change could have serious consequences. Unless alternative work can be found for the rural workforce, the rate of rural depopulation will increase and the social and economic cost to Australia will be substantial.

Long term sustainability

Arguably, the most important consequence of the new genetic technologies will be a major reduction in animal genetic diversity. It is inevitable that all livestock industries will make use of fewer breeding animals in the future. This move has already occurred in the poultry industry and is well underway in the pig and dairy industries.

At a global level, there has been a gradual reduction in the number of livestock breeds over the past two decades and the trend is accelerating. The availability of frozen semen and use of artificial insemination has led to many indigenous breeds being crossed and eventually replaced by the so called improved breeds. However, such indigenous breeds have had to rely on their genetic attributes to survive disease, parasites, climatic stress and sub-optimum nutritional conditions. It would seem logical that the new genetic techniques be used to identify the genes responsible for these characteristics. However, this is unlikely to occur at more than a modest rate and many of the genetically interesting breeds will have been lost in the meantime.

There is a perception that the use of clone lines of genetically superior animals will lead to a drastic reduction in the gene pool. The extent to which this will happen will depend on how many clone lines are used in production. One can envisage a large number of clone lines being required to meet the wide array of production systems and markets. On one hand, if the quest for improved strains is continued, these families will be continually replaced by new improved lines. On the other hand, the cost of evaluating new clone lines will restrict the scale of ongoing production and testing. Thus a reduction in size of the gene pool is inevitable. Of greatest concern is the need to retain access to new gene pools if breeding objectives or production systems change, eg if intensive rearing of pigs is banned. Under such circumstances, it would be desirable to screen a gene bank in the form of conserved germplasm as a starting point for new gene variants.

Ethical issues

Genotype based selection does not raise any new ethical issues since, like conventional breeding, it exploits natural genetic variation However, gene transfer has the capacity to generate new genetic variants, in some cases by moving genes across species barriers and there are concerns about unpredictable consequences, eg "genetic freaks".

Much has been written about the ethics of gene transfer in terms of the consumption of genetically modified products. Fortunately the commercialisation of genetically modified foods from non animal sources has helped to foster informed public debate. Indications are that food safety per se is the major consumer issue rather than whether the food product is of transgenic origin. On the other hand, recent experience in Australia where transgenic pigs with a promoter sequence of human origin were barred from release suggests that consumers want their food to be "pure".

Whilst genotype based selection exploits 'nature generated' gene variants, the use of *in vitro* reproductive techniques has raised ethical issues. For example, some sectors of the community will regard the surgical collection of oocytes from juveniles or foetuses as unnecessary and unethical. Other groups will be concerned about the prospect of large numbers of identical individuals being produced even as final production stock. Whether such technologies are judged to be ethical in the context of food production is of course a community decision, and a decision in which the view of scientists should carry no more weight than the view of any other citizen.

CONCLUDING REMARKS

Given the expected economic benefits from new genetic technologies, it is likely that industry will adopt them in some form. The livestock industries are under increasing pressure to modify products and change production practices, and new technologies will play an important role. However, in order to maximise the long term benefits, it will be essential that industry end users, scientists, genetic service providers and other stakeholders are all involved in technology development. In this way the negative impacts of the new technologies can be minimised. Widespread consultation at the development stage will not only ensure that the technologies are designed to meet the needs of end users, but that adoption and acceptance by all stakeholders will be expedited and sustained.

REFERENCES

ANDERSSON, L., HALEY, C.S., ELLERGREN, H., KNOTT, S.A., JOHANSSON, M., ANDERSSON,

K., ANDERSSON-EKLUND, L., EDFORS-LIJA, I., FREDHOLM, M., HANSSON, I., HAKANSSON, J. and LUNDSTROM, K. (1994). *Science 263:* 1771-4.

ARMSTRONG, D.T., HOLM, P., IRVINE, B., PETERSEN, B.A., STUBBINGS, R.B., McLEAN, D., STEVENS, G. and SEAMARK, R.R. (1992). *Therio. 38: 667-78.*

CAMPBELL, K.H.S., McWHIR, J., RITCHIE, W.A. and WILMUT, I. (1996). *Nature 380: 64-6*

CHARLIER, C., COPIETERS, W., FARNIR, F., GROBET, L., LEROY, P., MICHAUX, C., MNI, M., SCHWERS, A., VANMANSHOVEN, P., HANSET, R. and GEORGES, M. (1996). *Mammalian Genome* (in press).

COCKETT, N.E., JACKSON, S.P., SHAY, T.L., NIELSEN, D., MOORE, SS., STEELE, M.R., BARENDSE, W., GREEN, R.D. and GEORGES, M. (1994). *Proc. Natl. Acad. Sci. USA* **91:**3019-23.

EARLE, C.R., IRVINE, B.J., and ARMSTRONG, D.T. (1994). *Proc. Aust. Soc. Anim. Prod. 20: 428.*

FIGUEIREDO, J.R., HULSHOF, S.C.J., VAN DEN HURK, R., ECTORS, F.J., FANTES, R.S., NUSGENS, B., BEVERS, M.M. and BECHERS, J.F. (1993). *Therio. 40: 789-99.*

FUGII, J., OTSU, K., ZORZATO, F., DE LEON, S., KHANNA, V.K., WEILER, J.E., O'BRIEN, P.J. and MACLENNAN, D.J. (1991). *Science 253: 448-5* 1.

GEORGES, M., DIETZ, A.B., MISHRA, A., NIELSEN, D., SARGEANT, L.S., SORENSEN, A., STEELE, M.R., ZHAO, X., LEIOPOLD, H., WOMACK, J.E. and LATHROP, M. (1993a). *Proc. Natl. Acad. Sci. USA 90:* 1058-62.

GEORGES, M., DRINKWATER, R., KING, T., MISHRA, A., MOORE, SS., NIELSEN, D., SARGEANT, L.S., SORENSEN, A., STEELE, M.R., ZHAO, X., WOMACK, J.E. and HETZEL, J. (1993b). *Nature Genetics 4:* 206-11.

GEORGES, M. and MASSEY, J.M. (1991). *Therio. 35:* 151-9.

GEORGES, M., NIELSEN, D., MACKINNON, M., MISHRA, A., OKIMOTO, R., PASQUINO, A.T., SARGEANT, L.S., SORENSEN, A., STEELE, M.R., ZHAO, X., WOMACK, J.E. and HOESCHELE, I. (1995) *Genetics* **139: 907-20.**

HETZEL, D.J.S. (1993). *Nature Genetics 4: 327-8.*

KINGHORN, B., VAN ARENDONK, J., and HETZEL, J. (1994). *AgBiotech News and Information 6:* 297N-302N.

KLUNGLAND, H., VAGE, D.I., RAYA, L.G., ADALSTEINSSON, S. and LIEN, S. (1995). *Mammalian Genome 6: 636-9.*

MOLLER, M. (1995). PhD dissertation, Swedish University of Agricultural Sciences, Uppsala.

MONTGOMERY, G.W., CRAWFORD, A.M., PENTY, J.M., DODDS, K.G., EDE, A.J., HENRY, H.M., PIERSON, C.A., LORD, E.A., GALLOWAY, S.M., SCHMACK, A.E., SISE, J.A., SWARBRICK, P.A., HANRAHAN, V., BUCHANAN, F.C. and HILL, D.F. (1993). *Nature Genetics* 4: 410-4.

O'BRIEN, S.J., WOMACK, J.E., LYONS, L.A., MOORE, K.J., JENKINS, N.A. and COPELAND, *N.G.* (1993). *Nature Genetics 3:* 103-12.

PALMITER, R.D., BRINSTER, R.L., HAMMER, R.E., TRUMBAUER, M.E., ROSENFELD, M.G., BIRNBERG, *N.C.* and EVANS, R.M. (1982). *Nature 300:* 61 l-5.

PURSEL, V.G., PINKERT, C.A., MILLER, K.F., BOLT, D.J., CAMPBELL, R.G., PALMITER, R.L. and HAMMER, R.E. (1989) *Science 244:* 128 l-88.

REICHMANN, K.G., DRINKWATER, R.D., HETZEL, D.J.S., HIELSCHER, R.W. and HEALY, P.J. (1994) *Proc. of the 5th World Congress on Genetics Applied to Livestock Production* **21: 165-8.**

REXROAD, C.E. JR. (1992). *Anim. Biotech.* **3(1):** 1-13.

ROGERS, G.E. (1995). *Proc. Aust. Assoc. Anim. Breed. Genet.* **11:** 362-70.

ROTHSCHILD, M.F., JACOBSON, C., VASKE, D.A., TUGGLE, C.K., SHOT, T.H., SASAKI, S., ECKARDT, G.R. and McLAREN, D.G. (1994). *Proceedings of the 5th World Congress on Genetics Applied to Livestock Production* **21: 225-8.**

SCHLIEBEN, S., ERHARDT, *G.* and SENFT, B. (1991). *Animal Genetics 22: 333-42*

SCHWENGER, B., SCHOBER, *S.* and SIMON D. (1993). *Genomics* **16: 241-44.**

SHARMA, A., MARTIN, M.J., OKABE, J.F., TRUGLIO, R.A., DHANJAL, N.K., LOGAN, J.S. and KUMAR, R. (1994). *Bio/Technology* **12: 55-9.**

SHUSTER, D.E., KEHRLI, M.E. JR., ACKERMANN, M.R., and GILBERT, R.O. (1992). *Proc. Natl. Acad. Sci. USA* **89: 9225-9.**

WARD, K.A., LEISH, Z., BONSING, J., NANCARROW, C.D. and BROWNLEE, A.G. (1995). *Proc. Aust. Assoc. Anim. Breed. Genet.* **11: 371-8.**

WRIGHT, G., CARVER, A., COTTOM, D., REEVES, D., SCOTT, A., SIMONS, P., WILMUT, I., GRANER, I., and COLMAN, A. (1991). *Bio/Technology 9: 830-4.*