NEW TECHNOLOGY FOR GENETIC IMPROVEMENT OF LIVESTOCK

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ABSTRACT

As the pig industry faces increasingly uncertain fortunes, the revolution in the science of genetics continues to gather pace. The challenge will be to judge the extent to which the new technologies can help the industry in the light of public reaction. Today DNA *microarrays* the size of a microscope slide can be used to test 30 000 genes at a time to show whether they are "switched on" in a given tissue. Prospects are therefore good for identifying any individual genes that might be useful in improving meat quality and disease resistance. Gene transfer (GM) remains difficult and risky, but may be rendered unnecessary by the science of *functional genomics* which will allow control of the expression of the animal's own genes. Genomic *imprinting* could allow genes for fatness and longevity in the dam that are not expressed in her slaughter progeny. There are good prospects for using antibodies in semen to produce a single-sex slaughter generation. In a few years advances in reproduction may allow the entire genetic selection process to take place using only sperm and eggs, without any live animals. Combining for example the *myostatin* gene with Meishan cross sows and semen sexing could improve production efficiency by up to 30%. Breeding organisations must balance research effort between present and future technologies. The correct strategy involves three priorities: (1) maintain maximum improvement using present BLUP technology, (2) ensure maximum expression of existing genetic potential by good nutrition, and (3) evaluate and be prepared to deploy the new molecular technologies if required for industry survival.

INTRODUCTION

For more than thirty years the partnership between genetics and nutrition has led to dramatic improvements in the efficiency of pig production. Selective breeding with the aid of computers has raised the genetic potential for lean growth, while nutrition has sought to ensure that the increased potential is realised on the farm. These technologies are well proven, acceptable to the public, and highly cost effective. They are extensions of traditional methods offering steady improvement for years to come.

However within a very short time this comfortable picture could be radically changed by the current revolution in biotechnology. The Year 2000 has already seen the first cloned pigs and the complete DNA sequence for the human genome. At present these technologies are both expensive and controversial. Yet in the longer term they offer the prospect of cheaper, healthier and safer pork. Taking the pig industry as an example, this paper reviews the new

genetic technologies, and examines their role in improvement programmes along with the implications for animal nutrition.

STATISTICS AND INFORMATION TECHNOLOGY

For over ten years cheap desktop computer power has allowed the application of BLUP (best linear unbiased prediction) in pig selection. By using family records this gives more accurate prediction of genetic merit for traits of low heritability, doubling the rate of improvement for example in litter size. However the greatest contribution of BLUP has been that, together with AI acting as the genetic link, it allows direct comparisons of genetic merit among animals measured in different environments. This ability to compare across herds has opened the way for larger more geographically diverse nucleus populations, greater selection differentials, and faster improvement.

Shipping breeding stock from a nucleus in one country for production in another is costly in terms of transport and health security, and runs the risk that market requirements may be very different. The solution is to establish separate nucleus populations in key countries selected for local objectives. Where necessary BLUP calculations now can be easily conducted on data transmitted over the Internet using centralised statistical expertise. New genotypes can be introduced via frozen semen or embryo transfer.

This decentralisation also brings the challenge to bring down overhead costs by reducing the size of each nucleus population. Conversely the more accurate the selection the faster the rate of inbreeding. Procedures are therefore now being developed to combine a BLUP prediction of merit with a measure of inbreeding to give a single selection criterion which balances the two (Grundy *et al*, 2000). Nevertheless BLUP does not overcome the problem that traits such as meat quality or disease resistance are difficult to measure in the live animal.

COMPOSITE LINES

Substituting a better breed or line will always be a faster method of genetic change than selection. After 30 years of intense selection, some populations of the traditional breeds such as Large White and Landrace are becoming very homozygous. Incorporating a third breed such as the Duroc to restore heterosis and hardiness in a cross greatly adds to the overhead nucleus cost. The dilemma is that unless populations of sufficient size can be maintained, the minority breeds will quickly fall behind.

The solution has been to combine the attributes of different breeds in new composite lines. For example, Cotswold has introduced 25% of its White Duroc line into each of Large White and Landrace type dam lines to give new composite lines. When crossed together these give a parent gilt containing 25% Duroc from two rather than three nucleus lines. The two larger nucleus populations result in faster selection. They are also cheaper to maintain, with better physical condition than pure breeds due to residual heterosis from the Duroc. Multipliers too benefit from heterosis in what would otherwise have been a purebred GP (GrandParent).

The Chinese Meishan offers eight extra pigs per sow per year, accompanied by very poor growth and carcase characteristics. Since 1987 Cotswold has been developing a 50% Meishan composite dam line by selection for lean growth. Trials at Cotswold's UK R & D Centre in alliance with Imperial College at Wye (London University) show an advantage for the resulting 25% Meishan parent females over non-Meishan parents of 3.8 piglets weaned per sow per year. Backfat of the resulting 12.5% Meishan progeny was increased by 0.7 mm on *ad lib* feeding to 95 kg live weight, feed efficiency was 1% worse and there was no difference in growth rate. Work continues to improve uniformity and lean distribution.

GENOME MAPPING

Completion of the human genome map will greatly accelerate understanding of the mechanism of inheritance at the level of DNA. In the pig the DNA is distributed over 19 pairs of chromosomes and organised into some 100 000 functional genes. The DNA code is made up of sequences of the four bases (A, C, G, T) and a typical gene would be some 5-20 thousand bases in length. Once the sequence for a gene is known, its presence can be detected using a DNA test as in the case of the halothane gene.

Research teams from the USA and Sweden as well as the EU-funded Pig Genome Mapping Project (PiGMaP) are collaborating to map the genome of the pig (Visscher and Haley, 1998). By locating genes on the chromosomes, the objective is to understand how genes are organised and interact with each other, and how they affect all aspects of performance. To date some 2000 DNA sequences showing genetic variation have been placed on the pig maps. These maps are freely accessible on the Internet, along with similar maps for cattle, sheep and chickens.

MARKER GENES

Most quantitative traits such as growth rate are controlled by many hundreds of genes, each with a small effect. A gene with a large effect such as the halothane gene is very much the exception. Nevertheless, much research is now under way to identify possible genes with useful effects on performance. The function of most of the genes so far detected is unknown. They may however be situated on the chromosome close to a gene that does affect performance, for example growth rate, but for which no DNA test exists. Due to genetic linkage, the gene which can be detected will then show an association with growth rate, which is actually caused by its neighbour.

In this case, the DNA tested gene is known as a *marker*, because it marks a section of chromosome affecting performance. The gene whose presence it detects is known as a *quantitative trait locus* (QTL), with linkage between the marker and the QTL (Figure 1).

Possible markers have been reported for all the important traits, and many have been mapped. The 'hot spots' from world-wide pig research are shown in Figure 2. Hot spots for litter size exist on chromosomes 1, 8 and 16; lean growth on 4 and 7; and meat quality on 1, 6 and 15.

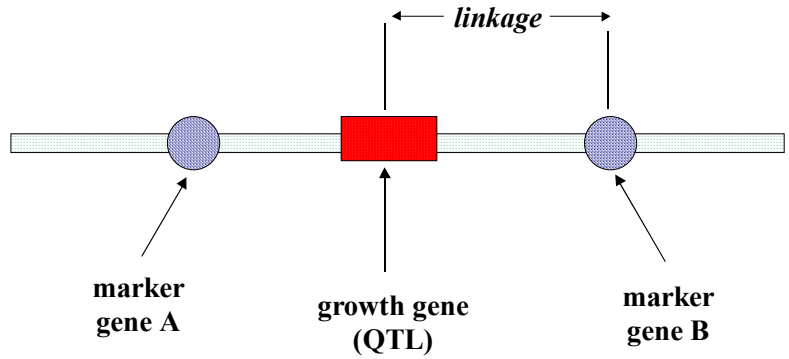

Figure 1. **Flanking marker genes A and B used to predict the presence of a growth gene or QTL (*quantitative trait locus*).**

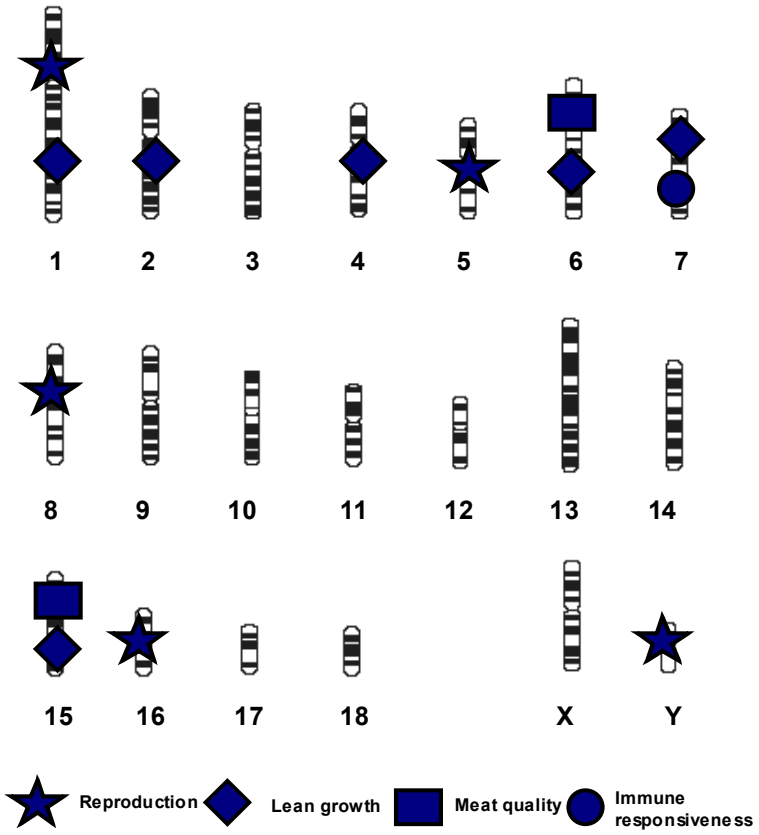

Figure 2. **Hot spots on pig chromosomes affecting reproduction (*Courtesy of P R Bampton*).**

MARKER ASSISTED SELECTION

In the process of *marker assisted selection*, DNA testing for the marker can be used to increase the frequency of the QTL and lead to an improvement in a production trait. The main benefit would be in traits such as meat quality or disease resistance which are difficult or expensive to measure in the live pig, or in reproduction which occurs late in life in one sex only. There are however a number of problems:

- DNA testing is still relatively expensive in relation to the small benefits of most markers on performance.
- There is no further benefit after the marker has been made homozygous
- Marker effects are often inconsistent between lines and even families
- Due the high number of candidates and traits, there is a statistically high chance of false positive markers. Already the number of markers reported would explain more than 100% of the genetic variation for some traits.
- Selecting on markers causes a loss of selection on other traits.
- Markers may have unknown harmful as well as beneficial effects. There may therefore be good reasons why selection has not fixed apparently favourable QTLs at 100% in these populations.

Current thinking is that the interaction of genes with each other is probably more important than originally recognised, so the implications of changing the frequency of any gene with a large effect may be difficult to predict from one population or even family to the next. A further difficulty is that the information from hundreds of markers of small effect may be difficult to collate. At this stage, the use of markers is therefore risky, whereas BLUP selection is already proven and cost-effective.

MARKER ASSISTED INTROGRESSION

As an alternative to selection within a line, a marker can be used to introduce a QTL from one line into another by *marker assisted introgression*. Suppose for example that a single gene for prolificacy is to be introduced from Meishan into Landrace. An F1 cross of the two is then backcrossed to Landrace over several generations, gradually increasing the proportion of Landrace while selecting for the desirable gene. In the absence of a DNA test, this is the method by which Cotswold introduced the dominant white coat colour gene from the Large White into its White Duroc line.

By the same principle other markers can be used to reduce the proportion of background genotype from the undesirable line, for example fatness from Meishan, hastening a commercially viable result. A further application might be the use of markers to retain maximum heterozygosity in any closed population. The risk of introgression is that it takes several generations. During this time the linkage with the marker could break down, selection on other traits may be lost, and the intermediate Meishan crosses could be over-fat and costly. The benefit of the QTL in improved performance would therefore need to be large.

NEW TYPES OF MARKERS

The main disadvantage of existing markers is their high cost and low accuracy. The majority are random segments of DNA of the form CACACA (*microsatellites*) that show genetic variation in the number of repeats. The inaccuracy stems from the weakness of the linkage in predicting the presence of the QTL. Either closer markers are needed or ideally a method of detecting the QTL directly. Several new options are now appearing:

- **AFLPs** Amplified fragment polymorphisms can be generated by enzymes which cut the chromosomes only at specific sequences. The presence of different genes results in DNA fragments of different length, which can be correlated with performance traits. Patented by KeyGene NV in the Netherlands and applied in plants, this has the advantage of producing a set of markers specific to one line. It also overcomes any patents on published markers.

- **SNPs** Single nucleotide polymorphisms are changes in a single specific coding unit of the genetic code. They are easy to detect and usually occur within the functional gene. Unlike microsatellites SNP tests can be automated on DNA *microarray* chips.

- **ESTs** Expressed sequence tags allow genes to be detected when they are 'switched on'. This would allow selection for animals expressing rapid early growth, earlier puberty, or perhaps for immune response. ESTs will provide the key to how genes are organised and controlled.

As the number of mapped genes increases, AFLPs are likely to provide alternative markers for QTLs or hot spots that are already known. *Microarray* technology already allows 30 000 SNP DNA tests to be conducted on a single chip the size of microscope slide, making this the most likely method for the future. This technology is therefore likely to be both powerful and cheap.

CANDIDATE GENES

Rather than searching at random for markers, the candidate gene approach uses knowledge of physiology to identify likely QTLs with a major effect. Equally, QTLs from human, mouse or other species maps would be candidates for investigation in the pig. Patents have been filed on some markers, but can often be overcome using others that are near to the QTL.

The halothane gene RYR1 appears to be the functional gene or QTL responsible for all the effects on lean growth and stress susceptibility. In Germany Cotswold has developed a very lean Pietrain-type composite sire line which is approaching homozygosity for the absence of the halothane gene. The oestrogen receptor ESR which affects litter size in some populations but not others appears to be a marker rather than the QTL responsible. H-FABP was discovered to affect intramuscular fat in Durocs and is currently being trialed under licence in other populations (Gerbens *et al.*, 1998). Candidate genes to control boar taint arising from skatole and androstenone are being investigated by several groups (Davis and Squires, 1999).

As an example, Cotswold is co-sponsoring a study at Glasgow University in which a knowledge of myosin heavy chain muscle protein polymorphisms is being used to deduce likely sequences of DNA that could act as markers within the genes affecting eating quality (Beuzen *et al.*, 2000). Certainly markers represent an important opportunity to accelerate genetic improvement, and Cotswold is very actively continuing its programme of in-house evaluation with exploratory selection on a combination of markers and BLUP.

GENOMIC IMPRINTING

In violation of the simple laws of Mendel, the expression of some genes can be switched on or off in the progeny depending on whether the gene was transmitted through the mother or father. This process of *imprinting* occurs by methylation of C (*cytosine*) units in promoter regions of genes carried by either sperm or eggs, shutting off their function. It may have evolved as a means of resolving conflicting requirements of mother and offspring. At least 34 genes showing imprinting are already known in the mouse (Ruvinsky, 1999).

In humans and mice the Igf2 gene (*insulin-like growth factor 2*) affecting growth appears to be maternally imprinted, and is thus expressed only when inherited from the father. By contrast, the corresponding receptor gene Igf2r is paternally imprinted and expressed only when transmitted by the mother. In pigs the Igf2 gene on chromosome 15 appears maternally imprinted and expressed only via the sire (Nezer *et al*, 1999). A marker for Igf2 in Pietrain crosses has been patented and is used by one breeding company. There have also been some reports of maternally imprinted genes for fat in the pig. This would allow higher levels of fat in the dam, allowing a long reproductive life, with no adverse effect on the carcase fat of the commercial progeny.

GENE TRANSFER

Gene transfer in animals between individuals and species has been possible for some years. The method of microinjection of DNA into the fertilised egg had a low success rate and could not control where and how many copies of the DNA sequence were incorporated. Dolly type cloning makes gene transfer much easier and cheaper, allowing DNA to be incorporated into cloned cells before transfer into the embryo. The first cloned pigs were announced by PPL Therapeutics in the USA this year.

First attempts to add extra copies of pig or human growth hormone genes brought adverse publicity due to undesirable effects on fertility and physical soundness. Methods are now being developed to control the number of copies, site of insertion, and the degree of expression. The technology of gene transfer is being driven by the use of the pig as a donor of hearts and other organs for humans (*xenotransplantation*). Human genes are added and pig genes 'knocked out' to avoid rejection of the heart as 'foreign'.

GENES FOR TRANSFER

What are the opportunities for gene transfer in pigs? Take as an example the *myostatin* gene, a naturally occurring mutation, which is the cause of double-muscling in Belgian Blue Cattle. When this gene is 'knocked out' of laboratory mice, lean growth rate is doubled and ham weight tripled (McPherron *et al.*, 1997). In a pure Meishan line with eight extra pigs per sow per year, a similar knockout might restore the very fat carcase to normal with dramatic consequences for productivity. Other opportunities might include:

- Lean growth (*e.g. leptin, Igf*)
- Boar taint (*e.g. androstenone, skatole*
- Meat quality *(muscle proteins)*
- Disease resistance *(major histocompatibility complex)*
- Gender determination *(SRY on Y-chromosome)*
- Pollution control (*e.g. phytase)*

Genes for androstenone and skatole might be knocked out to control boar taint. The SRY region has a major role in determining maleness. Transfer of this onto one of the non-sex chromosomes might allow sires which produce only male or female offspring.

Guelph University has produced pigs transgenic for phytase, which emit less phosphate pollution. In rats attempts have been made to introduce *cellulase* genes to improve digestion of plant material. This raises the issue of which genotype should be chosen for manipulation: the animal, the fodder plant, or the gut flora. The animal itself should probably be the last choice. An even better long-term solution will be to control the expression of the existing genes and avoid gene transfer altogether. This is a prime area where plant and animal geneticists could work together.

GENE THERAPY

Gene transfer involves a permanent change to the germ line by manipulation in the embryo. Gene therapy attempts to change the individual phenotype by adding genes to the tissues of the live animal, for example to replace an enzyme that is missing due to a naturally occurring mutation. These genes are not passed to the next generation. Genes can be introduced by a number of methods from injection to being fired through the skin adsorbed onto gold particles.

Researchers at the Baylor College of Medicine, Houston, have recently used this approach to introduce a modified GHRH (growth hormone releasing hormone) gene into the young pig (Draghia-Akli et *al*, 1999). The DNA sequence in the GHRH gene was altered to greatly extend its life by preventing normal breakdown by protease enzymes. The modified gene was introduced into three-week old pigs by a single injection. An electric current was then passed (*electroporation*) to integrate the DNA into the cells.

After 65 days the treated animals showed a 37% increase in growth rate with no penalty in body composition. In future the cost of such a treatment might well justify its use in

commercial production. While it would not be classified as GM, it would still be open to concerns of ethics and welfare for animals growing 'unnaturally' fast.

DISEASE RESISTANCE

This major source of loss in pig production has attracted strangely little genetic research. The existence of genetic variation in immune responsiveness within and between breeds has only recently been demonstrated. At Guelph, selection on a BLUP index for high or low immune responsiveness was successful in creating a genetic difference (Mallard *et al.*, 1992). At Iowa State, Durocs showed greater resistance to PRRS virus than other breeds (Halbur *et al.*, 1998).

However, a line with higher immune responsiveness would be expected to show a correlated reduction in lean growth every time the immune system was triggered (Baker and Johnson, 1999). This is a natural defense in response to infection, and is mediated by the cytokines such as interferon and interleukin. One challenge for molecular genetics would be to break this association so that high immune responders could continue to grow normally.

REPRODUCTIVE TECHNOLOGIES

Improvements can be expected in the reproductive technologies such as frozen semen, frozen embryos, and non-surgical embryo transfer (ET). As pigs already have large litters the main benefit of ET will be in establishing and updating nucleus populations, obtaining 100% of the desired genotype with minimum health risk. Cloning the slaughter generation would give 100% uniformity from top pigs in the nucleus, but cloning would need to be repeated each year to keep pace with genetic improvement. Genetic variation would of course need to be maintained in the nucleus to allow continued improvement by selection, which may well cause the nucleus to lag behind the cloned commercial population in genetic merit.

In vitro fertilisation (IVF) together with ET will be *enabling technologies* for gene transfer. *In vitro* meiosis to produce sperm and eggs would be the final step that would allow successive generations to be produced entirely *in vitro*. IVF would be used to produce cloned embryos from which cells would be sampled to conduct marker assisted selection. *In vitro* meiosis would then give the next generation of sperm and eggs directly from cells of the embryo allowing IVF to be repeated (Haley and Visscher, 1998). Genetic improvement could thus proceed at 5-10 times the pace without the need for any live pigs.

SEMEN SEXING

The idea of raising antibodies to remove unwanted X or Y sperm is not new. However, a recent breakthrough in Guelph now offers the prospect of a commercial method for doing this within 3-5 years. Based on the knowledge that the DNA on the X chromosome of all mammals is very similar (Ohno's Law), it assumes that proteins on the surface of the sperm must also be very similar between species. If so, then injecting male porcine material into a

male rabbit will not raise antibody to male-specific proteins, but will raise antibodies to non-sex-specific proteins. These antibodies can then be used to remove the non-sex-specific proteins, leaving the male-specific molecules available for retrieval. From these, sex-specific antibodies can be raised by injection into the opposite sex (Blecher *et al,* 1999). The plan is to prepare monoclonal antibodies that will be added in solution to the semen. Sperm of the unwanted sex can then be made to clump together and filtered off using glass wool.

The main benefit of semen sexing lies in improved feed efficiency and carcase lean content. Compared with a castrate, a gilt has up to 15% better feed efficiency and 3% more lean. An entire boar shows roughly the same advantage again over a gilt. For an industry practicing castration, switching to 100% gilts would give an annual advantage of over $60 per sow place. Switching to 100% entire boars could give over $180 per sow place. Single sex production also avoids the need for split-sex feeding, better meeting nutritional requirements and improving uniformity.

Through its owner Ridley Inc, Cotswold has made a strategic investment of $1 million in the Guelph University spin-off company Gensel Biotechnologies Inc set up to commercialise this process. The strategic investor for cattle is Genus, and Monsanto is a collaborator for protein biochemistry. If successful the semen sexing technique will be easy and cheap to apply for on-farm AI collection. It involves no genetic manipulation, and is safe and acceptable to the public. In the short term sex determination probably represents the greatest single potential step forward in pig production and is therefore well worth the risk. The slower method of physically sorting stained sperm by laser (*flow cytometry*) would not be fast enough to supply the high numbers of sperm per insemination in pigs.

FUTURE GENETIC OBJECTIVES

The pig industry will continue to compete on the low cost per kilo of lean meat. With the move to larger more integrated production pyramids serving specific needs of retailers, there will be increased emphasis on the quality and uniformity of the meat. The way meat is produced will come under closer public scrutiny, including of ethics, naturalness, traceability, the environment, sustainability and animal welfare.

In the pig industry today arguably some 20-30% of genetic potential is not realised on the farm. There are two main reasons for this. The first is poor herd health, with multifactorial diseases such as porcine respiratory syndrome in which PRRS, ‘flu and pneumonias act in concert. The second reason is *incomplete knowledge or application of the nutritional needs of the modern improved genotype*. Genetic objectives are therefore twofold: to continue to raise genetic potential, but also to increase the probability that this potential can be realised on the farm.

A GENETIC CHALLENGE FOR NUTRITION

Genetics and nutrition will need to work together in three areas. First, the nutritional requirements of the modern pig must be understood and met more closely. Second, the correct choice of selection objectives for future improvement will depend on a better understanding on the biology of the pig. Third, the potentially large changes in lean growth, offered for example by the *myostatin* gene, must not be attempted without a nutritional strategy to exploit them.

Taking a simple view, the daily feed intake of a pig is converted to product in the form of saleable lean and fat. In the past, pigs have been fat because daily intake exceeded daily lean deposition. The ideal animal for *ad libitum* feeding would need to have its feed intake genetically linked to lean growth potential (a genetic correlation of 1.0). Serial dissection studies on Cotswold sire lines suggest that dissectable lean growth rate is much higher than expected in the young growing pig, exceeding 400 g per day by 40 kg live weight. This means that before about 60 kg live weight feed intake is the limiting factor, but after 60 kg genetic potential for lean deposition is limiting.

Trials now under way at Cotswold's UK R & D Centre (Wye) suggest that boosting energy and protein levels by 5% above current commercial practice can increase lean growth rate by 10% with very little increase in fat. Increasing the energy alone and leaving the protein unchanged seems to give 90% of this increase. This confirms the view that energy intake rather protein intake is the limiting factor in the early growth of the modern pig (de Lange, 1997). With continued genetic improvement of lean growth potential, and in the absence of a matching increase in feed intake, one of the greatest challenges for nutrition will be to formulate an affordable diet which can actually supply this early energy requirement.

NUTRITION AND BREEDING OBJECTIVES

With no sign of a decline in genetic variation, selection can be expected to continue to increase lean growth at the present rate for some years. Up to now, feed efficiency has largely been improved by substituting lean for fat. As pigs become leaner, further improvements in efficiency will increasingly depend on raising the rate of lean growth itself. The longstanding question remains of how much selection emphasis if any should be placed on voluntary feed intake. Is it realistic to expect intake to increase as a consequence of selection on lean growth?

In practice it appears that lean growth potential and feed intake are highly dependent on diet, health and other environmental conditions. For example, feeding a whey-based liquid diet can far exceed what seemed to be the maximum lean growth on the highest-quality solid diet. The concept of a genetic potential level for lean growth and intake therefore only appears useful for a specific set of husbandry conditions. The excellent long-term study in Edinburgh confirms the existence of genotype x nutrition interactions in lines selected for different objectives (Cameron, 1997).

Certainly it appears that a genetic increase in early feed intake is required, but with very little increase beyond 60 kg. In lean genotypes, intake is very highly genetically correlated with growth rate. Increased early intake is therefore most easily achieved by increasing the selection emphasis on early versus late growth. It is not necessary to incur the expense of individual measures of feed intake by using electronic feeding stations. Genetic improvement can only proceed alongside the appropriate nutritional changes: *genetics and the environment must change together.* Computer models allow alternative strategies to be evaluated.

PUTTING THE TECHNOLOGY TOGETHER

The new technologies could be brought together to revolutionise the pig industry. Suppose for example that a Meishan type containing the *myostatin* knockout could give single line production with an acceptable carcase and 32 pigs per sow per year. Semen sexing could be used to give 100% entire male offspring, and androstenone/skatole knockouts could remove boar taint. This would immediately improve production efficiency by some 30%.

Another possibility would be to produce surrogate mothers from an F1 cross of say Meishan with Fengjing. These would receive cloned and frozen embryos from a dedicated sire line containing *myostatin*. Dam lines would be bred only for uterine capacity and the sire lines only for slaughter pig attributes. As well as 32 pigs per sow per year this could give better lean growth with faster genetic improvement of finishing traits.

Of course no one is advocating these methods, but their adoption by rival industries could pose a threat in terms of lower production cost. On the other hand there could be a huge benefit for the animal and human by manipulating genes for say disease resistance or sustainability.

RISKS OF GENETIC MANIPULATION

So what are the risks of gene transfer in animals? The nightmare scenario would be genetic modification of pathogens (bacteria or viruses) which might then cause an epidemic, perhaps lethal, in man or across a range of species. Production of toxins or allergens would be relatively easy to avoid on any scale by judicious trials in advance of widespread release. Any accident causing sterility would of course be self-eliminating. Risks to animal welfare clearly exist from production stress or physical malfunction. Whilst these risks are very small, those involving pathogens at least have the potential to affect a much larger proportion of the population than say mountaineering or air travel.

The real risk surely lies in the fact that our knowledge of the molecular mechanisms of inheritance, and particularly of the way genes interact with each other, is still rudimentary. Sexual reproduction is set up to produce new genetic variation and is therefore inherently unpredictable. It is therefore difficult to predict the consequences of inserting a gene with 100% certainty. In the event that some undesirable genetic transformation did occur, there is the danger that the knowledge needed to avert a disaster would simply not exist. The *prion*

factor causing BSE and the absence of a solution to cancer would be seen by some as examples of gaps in knowledge. As soon as there is complete understanding of the mechanisms of gene action, the risk will evaporate.

FUTURE GENETIC STRATEGY

So what strategy should be adopted for future genetic improvement and research? There are three components:

- Maintain maximum rates of improvement using existing BLUP methods.
- Close the gap between genetic potential and actual performance on farm.
- Secure access to the new technologies and be prepared to quickly deploy them if required to defend the competitive position of the industry.

To close the achievement gap Cotswold has a large investment in better understanding the nutrient requirements of modern genotypes, especially of the young growing pig where energy intake may be limiting lean growth. There is also a need to increase research on the immune system of the pig.

To access the new technologies Cotswold has developed an international science base run by its five full-time PhD geneticists. As well as in-house research this is supported by research fellowships and alliances, collaborative research agreements and research contracts with biotech companies, and shareholdings in semen sexing company Gensel and DNA typing company Rosgen. The aim is to be closely informed on new ideas and technology with the opportunity for early experimentation where appropriate.

SOME CONCLUSIONS

Through gene mapping, gene therapy, gene transfer, and the control of gene expression, the new technology of molecular genetics has the potential to revolutionise the process of livestock breeding. Today the main contribution of genetic maps and markers is to understand how genes operate. Methods of gene transfer are being developed for medical applications and will inevitably become available to the livestock industry. As these new methods are being evolved, it is important to realise that modern selective breeding programs have been both successful and cheap.

In pigs the immediate challenge for genetics and nutrition is to deliver to the farmer a higher proportion of the genetic potential for lean growth that already exists. The next challenge is to provide diets that can meet the nutritional requirements at ever increasing rates of growth. To help the breeder choose the correct objectives for genetic change, more understanding will be required of the basic biology of pig growth, and in particular factors determining feed intake.

For the pig industry the goal remains the production of high quality lean meat at minimum cost, but with increasing regard for public approval, animal welfare, wholesomeness and the environment. The breeding companies will be integrators of a range of technologies, providing a package of genetic services to the food chain of which a full knowledge of nutritional requirements will be an integral part. At this stage the knowledge does not exist to fully assess the risks of genetic manipulation in livestock. In the meantime genetics and nutrition must work together to ensure that the industry has access to whatever new technology is needed to compete in the future.

From fertilized egg to newborn, thousands of genes twinkle on and off in the delicate dance of creation.

(Huang, 2000)

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