COMPONENTS OF THE SOMATOTROPIC AXIS AS PREDICTORS OF GENETIC MERIT FOR GROWTH

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SUMMARY

Compelling evidence for the genetic regulation of some components of the somatotropic axis is presented using information gathered from a variety of animal models. Currently, a simple measure of circulating ST that shows a consistent association with genetic merit for growth is not available. Furthermore, there is a need to elaborate on the various physiological and metabolic functions of somatotropin (ST) to ensure that modification of circulating ST levels by selection does not have undesirable effects on other production traits. Insulin-like growth factor-1 (IGF-1) appears to be a useful physiological predictor of genetic merit for growth. While selection for higher plasma levels of IGF-1 in mice has resulted in higher growth rates, particularly around puberty, it has also caused an increase in mature body size. This may not be desirable in an animal production system due to increased feeding costs to support the breeding population. However, initial evidence would suggest that an associated increase in maternal reproductive capacity more than offsets the increase in mature body size. We conclude that plasma levels of IGF-1 warrant further examination as an aid to increasing the rate of genetic gain in growth.

INTRODUCTION

There are numerous reports in the scientific literature extolling the virtue of selecting for increased growth rate in domestic animals. More recently, there has been a shift away from growth rate per se as a selection objective to objectives which include lean growth or efficiency of growth (eg Simm et al. 1988). This reflects changing consumer requirements and escalating costs of production, and it is likely that there will be further changes in selection objectives in the future. Therein lies a problem for farmers or companies who produce seed-stock. If selection objectives undergo regular change, there will be little opportunity to genetically modify the population when annual rates of change are only 3% or less. Improved reproductive technologies may enhance rates of genetic change (eg Smith, 1986) and the use of recombinant DNA techniques to produce transgenic stock may improve flexibility (eg Pursel et al. 1989), but it is unlikely that such techniques will solve the problem on their own.

An additional approach to those mentioned above is to search for physiological traits that may enhance the rate of genetic change by increasing the accuracy of selection, increasing the selection intensity or decreasing the generation interval. As noted by Robertson (1987), this approach has yet to provide any startling results which may not be surprising given the multitude of pathways that regulate growth or any other trait of economic interest. It would therefore seem likely that an index of physiological traits (possibly including the production trait) will be required to exceed the rate of genetic gain currently achievable. It is also likely that modifications to existing theory or even new approaches may be required to obtain the full benefits of using physiological indicator traits. Of particular importance will be the interpretation of genetic and environmental components. At the physiological level, many environmental effects may themselves have inherited components. For example, levels of some hormones will be controlled directly by gene action but also indirectly by other regulatory hormones which are influenced by both genetic and environment effects. This is clearly analogous to the widely accepted maternal effects model, the difference being that, with the physiological traits, the expression of the various genotypes is in the same animal rather than in separate generations.

Many hormones are known to be involved in the regulation of growth and thus could be considered as potential predictors of genetic merit for this trait. However, the most promising area of research in this regard involves components of the somatotropic axis. The central hormone of this axis is somatotropin (growth hormone) which is secreted in a pulsatile fashion by the pituitary gland. This secretion is stimulated by growth hormone releasing factor (GRF) and inhibited by somatostatin (somatotropin release inhibiting factor, SRIF). While somatotropin appears to have some direct effects on the growth process, many of its actions are mediated by the insulin-like growth factors, or somatomedins. Insulin-like growth factors 1 and 2 (IGF-1, IGF-2) are small peptide hormones secreted into the circulation by some organs (notably the liver) under the influence of somatotropin, but also produced and acting locally in many tissues of the body.

The key role of the somatotropic axis in regulating growth has been known for many years. Hypophysectomy (removal of the pituitary gland) in young animals markedly retards growth, but normal growth rates can be achieved by treating hypophysectomised animals with somatotropin (ST) Olson et al, 1981). Furthermore, administration of ST to intact animals has been shown to enhance growth rate, protein deposition and feed conversion efficiency, and decrease carcass fat content (see Bauman and McCutcheon, 1986; Gluckman et al. 1987).

The purpose of this paper is to discuss evidence for involvement of the somatotropic axis in the genetic regulation of growth and to evaluate the possible use of components of the axis as predictors of genetic merit.

The Somatotropic Axis and Genetic Regulation of Growth

Several types of animals have contributed to our understanding of the genetic basis of components of the somatotropic axis and their role in regulating growth. For convenience these have been categorised as: animals carrying major genes, divergent breeds, selection lines and transgenic stock.

Major gene effects A number of inherited growth disturbances have been identified in humans, domestic animals and laboratory species. In some instances, the endocrine nature of these disorders has been identified. Table 1 presents some examples of growth disturbances controlled by major genes and their known status with respect to components of the somatotropic axis. Physiological studies of some of these major genes have helped to establish the importance of components of the somatotropic axis in regulating normal growth. It is apparent from Table 1 that the endocrinological expression of these major genes may differ. Thus, for example, injection of ST into ST-deficient mice has been shown to increase levels of IGF-1 and to increase growth (eg Holder et al, 1980) whereas, tissues of Laron-type dwarfs are not sensitive to ST administration (Geffner et al. 1987). Clearly, these results implicate different components of the somatotropic axis as the source of particular growth disturbances. While these animals may provide useful information about the influence of various hormones on growth, they are not necessarily good models of growth in normal animals. This is because hormone levels may be outside the normal physiological range or there may be several physiological traits affected, making it difficult to trace the impact of any one hormone. However, Willeberg et al (1975) and Laron et al (1989) have both reported gene-dosage effects, in IGF-1 and ST-binding protein, respectively. Thus, animals heterozygous for some major genes may be of greater value for studying the genetic basis of the endocrine control of growth, since they indicate the magnitude of change in the hormone required to effect a change in growth, without the extreme aberrations characteristic of the homozygote.

The growth disturbances listed in Table 1 all result in reduced mature body size, except for mice carrying a major gene for rapid postweaning growth rate (Bradford and Famula, 1984). The hormonal basis of this increased growth has not yet been reported. However, Medrano (pers. comm.) has noted that immunoreactive levels of ST have consistently been lower in plasma and pituitaries of mice carrying the high growth gene. In contrast, plasma levels of IGF-1 have been consistently higher in

high-growth mice. Initially it might appear surprising that there are not more cases of "genetic giants". However, this most likely reflects the relatively strict regulatory mechanisms that exist amongst the various hormones controlling growth. Thus, if a mutation did result in the potential to markedly increase ST levels, the counteracting forces of increased SRIF and decreased GRF could effectively mask the phenotypic effects of the mutation. In contrast, the number of dwarf conditions that exist can be explained by the total absence of one or more of the regulatory mechanisms leading to a breakdown in the control of growth.

Table 1 Hormonal basis of some growth disturbances caused by major genes

Species	Common Name	Hormone Levels (PRL = Prolactin)	References[1]
Human	Pygmy	Normal ST, reduced IGF-1	9
	Laron dwarf	Elevated ST, reduced IGF-1	8
Mice	Snell dwarf	ST and PRL deficient, reduced IGF-1	2,5
	Little mouse	ST and PRL deficient, reduced IGF-1	5
	Pygmy mouse	Normal ST, IGF-1 and PRL	5
	Rapid growth mouse	Reduced ST, elevated IGF-1	4,12
Poultry	Sex-linked dwarf	Elevated ST, reduced IGF-1	3,7,11
	Autosomal dwarf	Normal ST and IGF-1	3,7
Dogs	German-Shepherd dwarf	Reduced ST and IGF-1	1,6
Rat	ST deficient rat	Reduced ST and IGF-1	10

[1] (1) Willeberg et al (1975), (2) Holder et al (1980), (3) Scanes et al (1983), (4) Bradford and Famula (1984) (5) Charlton (1984), (6) Eigenmann et al (1984a), (7) Huybrechts et al (1985), (8) Geffner et al (1987). (9) Merimee et al (1987), (10) Skottner et al (1989), (11) Tixier-Boichard et al (1989). (12) Medrano, U.C. Davis (pers. comm.)

Divergent breeds Breeds or strains within a species may provide useful information on genetic relationships between traits. However, this is limited to breeds that have recent common genetic backgrounds. If there is no common genetic background, apparent relationships between traits may be misleading compared with the true within breed relationship, which is generally of greatest interest.

The study of Eigenmann et al (1984b), which reported a close relationship between plasma IGF-1 concentrations and liveweight in various breeds of poodle, has been widely referenced. Furthermore, this study was the first to give an indication that the IGF-1/liveweight relationship may have a genetic component, other than where major genes for growth disorders are present. A further study by Eigenmann et al (1988) using different dog breeds is of little use for examining the genetic relationship between IGF-1 and liveweight because of the lack of recent genetic links between the breeds involved.

Studies by Buonomo et al (1987) and Lauteric et al (1988) used related breeds of poodles and/or pigs to further examine the genetic relationships between hormones of the somatotropic axis and growth. Hormones investigated included IGF-1, IGF-2, and ST as well as the ST binding protein.

While the relationships found were not entirely consistent, they tended to confirm the previous findings of Eigenmann et al (1984b) and of studies examining the effects of major genes. Unfortunately, there was little or no information regarding the nutritional status or sex of the animals or the number of sires or dams represented. These could have had a major impact on the results reported.

Generally, knowledge about the somatotropic axis gained from the study of divergent breeds would concur with that from the major gene studies. Low levels of IGF-1 tend to be associated with low liveweights and vice-versa. However, ST levels are not always closely related to body size. Differences in ST secretory patterns were sometimes detected, suggesting that a greater understanding of the significance of different patterns might prove useful.

Selection lines A seemingly obvious group of animals to examine for differences in the somatotropic axis are those from liveweight or body size selection experiments. Interestingly, few results from such studies have been reported. Ringberg Lund-Larsen and Bakke (1975) reported on ST and IGF-1 levels in 3 lines of pigs. Two of the lines had undergone 6 generations of divergent selection for an index based on liveweight gain and backfat thickness, while the third line was a randomly selected control line. The high and low lines were significantly different in circulating ST (based on one sample) and IGF-1. The low line also showed significantly reduced levels of ST relative to the control line. These results are encouraging since they provide evidence for a quantitative genetic relationship between liveweight gain and/or backfat depth and ST/IGF-1 levels. Current evidence would suggest that the difference in ST and IGF-1 levels has resulted from the liveweight gain component rather than the backfat component of selection. Recently, Norton et al (1989) reported on the ST status of 2 lines of pigs divergently selected for growth rate for 5 generations. Several methods of ST assessment showed the high growth rate line to have lower ST levels. Norton et al propose several arguments to explain this apparent contradiction, one being that animals having higher metabolic clearance rates of ST may be faster growing. The conflicting results of Ringberg Lund-Larsen and Bakke (1975) and Norton et al (1989) emphasise the need for greater understanding of the physiological processes regulating levels of hormones which might be used as potential indirect predictors.

Medrano and Bradford (Univ. of California, Davis; pers. comm.) have examined plasma levels of IGF-1 in two lines of sheep selected for high 120-day weight and in a randomly bred control line. At weaning, the selected lines were about 5.5 kg heavier than the control line. Only one of the selection lines showed higher plasma levels of IGF-1 relative to the control line.

Carter et al (1989) found no difference in IGF-1 levels between lines of Southdown sheep divergently selected for liveweight-adjusted backfat depth. Since there was no difference between the lines in growth rate, this result is not surprising. In the same study, ST levels were not significantly different between the lines while they were fed 30% above maintenance. However, when the animals were starved for 63.5 hours then refed, animals from the lean line were found to have higher plasma levels of ST. This result is consistent with the previously mentioned effect of exogenous ST on carcass composition. However, it is difficult to explain why the differences were apparent only during nutritional stress and following refeeding.

Transgenic animals A variety of transgenic stock have been produced incorporating genes that code for various components of the somatotropic axis. These include:

ST:	Palmiter et al 1982 (mice); Hammer et al 1985b (sheep, pigs, rabbits); Brem et al 1988 (pigs, mice); Vize et al 1988 (pigs); Pursel et al 1989 (pigs); Ward et al 1989 (mice, sheep),
IGF-1:	Cascieri et al 1988 (mice); Mathews et al 1988b (mice); Pursel et al 1989 (pigs), and
GRF:	Hammer et al 1985a (mice); Pursel et al 1989 (pigs).

When interpreting information from these studies, it should be remembered that the transgenic animals often exhibit chronically elevated levels of the hormone controlled by the transgene. In this respect, they provide the obverse of the previously mentioned major gene animals, where chronically

reduced levels of hormones are typically found. Also of importance is that transgenic stock often express the transgene in organs/tissues that would not normally do so. One consequence of this "ectopic" production is that the normal interplay between hormones within an axis is often absent so that, for example, feed-back mechanisms may not act in the usual manner. Finally, many of the gene constructs used are not based on the gene from the host species. In particular, human gene constructs are often used in domestic species and heterologous (cross-species) hormones may not act in the same manner as the homologous (natural) version of the hormone.

As mentioned previously, a number of groups have now reported the successful incorporation of the ST gene into mice, rabbits, sheep and pigs. Generally, faster growing and leaner stock have resulted. However, in farm species, the transgenics have often exhibited problems including infertility, constitutional faults, poor health and reduced lifespan.

Transgenic animals generally provide results consistent with our current understanding of the somatotropic axis and the interplay between its constituent hormones. Mathews et al (1988a) and Pursel et al (1989) reported that plasma levels of IGF-1 were elevated in mice and pigs, respectively, carrying various transgenes for ST. Elevated levels of ST were assumed to be responsible for the increased IGF-1 levels. Hammer et al (1985a) showed that mice carrying copies of a growth hormone releasing factor (GRF) gene had elevated ST levels and increased growth rates. Subsequently, Mathews et al (1988a) showed that descendants of these mice also have elevated IGF-1 levels. In contrast, Pursel et al (1989) did not find elevated levels of ST in pigs carrying multiple copies of a GRF fusion gene. Although not stated, it must be assumed that growth rate was not altered. Mice carrying copies of a human IGF-1 transgene were found to have elevated human IGF-1 levels and increased growth (Mathews et al, 1988b). However, endogenous production of ST and IGF-1 were severely down-regulated while SRIF levels remained unchanged.

Mathews et al (1988a) also examined the ontogeny of IGF-1 in relation to ST levels and increased growth in mice transgenic for rat ST and bovine ST. Elevated plasma levels of ST were found at birth but IGF-1 levels did not increase until 2 weeks of age and increased growth was noted at 3 weeks of age. This is consistent with previous findings that neonates are ST-insensitive. The transition to a ST-sensitive state is still not clearly understood but is likely to involve the delayed expression of ST receptors.

Studies of transgenic animals have provided additional information with respect to the genetic regulation of the somatotropic axis. However, it should be restated that the regulation of various hormones is not typical of that seen in normal animals. Hence, it would be unwise to base any conclusions with respect to genetic control of the somatotropic axis on information from transgenic stock alone.

COMPONENTS OF THE SOMATOTROPIC AXIS AS POTENTIAL PREDICTORS OF GENETIC MERIT FOR GROWTH

Somatotropin (ST)

Clearly ST has a central role in the regulation of growth as can be seen from studies of animals with severely depressed or chronically elevated levels of ST. As a consequence, ST would appear an obvious choice as an indirect predictor of genetic merit for growth. However, there are several reasons as to why ST may not be a good choice. First, it is well established that ST is released in a pulsatile fashion in most mammals. Therefore, it would be necessary to take a series of blood samples in the replacement stock to get a true profile of ST release. This is unlikely to be practical for most sire-breeders, although some large companies or cooperatives could implement such a scheme if the benefits were substantial enough. An alternative approach would be to treat replacement stock with GRF and measure pituitary sensitivity to this hormone (Norton et al, 1989), but the relationships between pituitary senstivity to GRF, circulating ST and genetic regulation of growth are yet to be

established. Regardless of whether a simple approach to measuring ST can be found, there may be other disadvantages in using it as a predictor. ST is involved in several physiological processes besides growth, and, until further research has clearly established these other effects (particularly on other economically important traits such as lactation), caution is required in promoting it as a potential indirect predictor of genetic merit. A final argument against the use of ST as an indirect predictor of genetic merit is the absence of genetic giants with elevated ST levels. A possible reason for this is that the ST down-regulating mechanisms are sufficiently robust to overcome any mutation allowing for excessive ST production. Some evidence in support of this theory is provided from studying animals transgenic for ST constructs. While such animals often have chronically elevated ST levels, their own (endogenous) ST production is virtually nil (Mathews et al, 1988a). The circulating ST in such animals appears to be produced by ectopic sites which presumably are not under the control of the normal regulatory pathways.

Insulin-like Growth Factor-1 (IGF-1)

IGF-1 does not appear to suffer from the deficiencies of ST in terms of a potential indirect predictor of growth. It is not released in a pulsatile fashion, shows little diurnal variation and its primary function appears to be mitogenic. Prior to the mouse selection experiments of Blair et al (1989) and Baker et al (1989), there was substantial evidence for a phenotypic relationship between IGF-1 levels and body size or growth but only limited evidence for a genetic relationship between these traits.

Roberts et al (1990) examined the ontogeny of circulating IGF-1, in male and female Romney sheep from about 5 to 17 months of age, in order to identify optimum sampling regimens for use of IGF-1 levels as a physiological predictor of genetic merit. The developmental patterns of IGF-1 were clearly different in the two sexes, with males showing a surge in IGF-1 concentrations at about the time they would be expected to reach puberty (about 7 months). In contrast, levels of IGF-1 rose more steadily in females until plateauing at about 11 months of age. From the time of the surge in IGF-1 in the males until the completion of the trial, there was a significant difference between the sexes in IGF-1 levels. Females which had exhibited oestrus by about 8 months of age had significantly higher IGF-1 levels (326 $\pm$ 16 ng/ml) than those which had not exhibited oestrus (249 $\pm$ 8 ng/ml). This effect remained significant after adjusting the two groups to a common liveweight. Intraclass correlations between the IGF-1 level at the first sampling and subsequent levels over a period of 12 months (20 samplings) ranged from .41 to .85. This indicated that IGF-1 levels in young animals were moderately to highly correlated with levels to 17 months of age, suggesting little benefit in multiple measurements of IGF-1 levels to assess an individual's phenotype. Throughout the trial, IGF-1 levels showed strong positive correlations with liveweight. The main conclusion of Roberts et al (1990) was that plasma levels of IGF-1 met several of the criteria for being a successful indirect indicator of growth, but that the genetic association between plasma IGF-1 levels and economically important traits was still largely unknown.

Other Hormones

Evidence for genetic variation in levels of other hormones (eg GRF, SRIF, the thyroid hormones, prolactin and others) and their covariation with growth is largely non-existent. Furthermore, circulating levels of some hormones (eg SRIF) may not be strongly related to their role in regulating ST secretion by the pituitary gland. Nevertheless, as additional information becomes available the potential of these hormones must be re-examined.

RESPONSES TO SELECTION FOR IGF-1

Mice

In 1985, divergent selection lines using plasma concentrations of IGF-1 at 6 weeks of age as the selection criterion were established at Massey University. To enable adequate quantities of plasma to be obtained for analysis, samples from 4 mice (2 of each sex) were volumetrically bulked to obtain an average litter value. This necessitated the use of family selection. Each selection line comprised 10 males and 20 females. Inbreeding accumulated at rates of 3.6% and 5.3% per generation for the high and low lines, respectively (Blair et al. 1989).

Divergence between the high and low lines accumulated steadily and yielded a realised heritability of .15 ± .12, based on family selection for 7 generations. Blair et al (1989) noted that this value was depressed because of reduced divergence between the high and low lines in the final 2 generations. Furthermore, substantial fluctuations in IGF-1 concentrations between generations (control mean ranged between 72 ng/ml and 133 ng/ml) made the comparisons of between generation differences difficult. Regardless of these difficulties, the trial showed that genetic variation did exist in plasma levels of IGF-1.

Studies based on mice from the IGF-1 selection lines have shown that significant differences in liveweight can be detected by 21 days of age and that these persist into maturity (Siddiqui et al 1990). At the age of selection, the high line typically exceeds the low line by between 20% and 25%. The greatest difference in growth velocity occurred between about 25 and 35 days of age. Subsequent to this age, growth velocities of the lines were not significantly different. This result would suggest a strong genetic link between plasma levels of IGF-1 and liveweight. A caveat must be applied to this result due to the unusual way in which liveweights in the low line declined dramatically in generation 5. However, a further 6 generations of random breeding has failed to uncover any major gene for depressed liveweight, which was a possible explanation for the sudden change. The size of the response in liveweight in relation to the change in plasma levels of IGF-1 raises the question of whether other physiological mechanisms have also been genetically modified.

Siddiqui et al (1990) carried out a serial slaughter trial in which they showed the water, fat and protein composition of mice from the 2 lines did not differ when compared at the same body weight. Selection for or against plasma levels of IGF-1 appeared to generate a coordinated change in the various body components. This is in contrast to several experiments in which selection for liveweight has often increased the proportion of protein in the carcass in the period prior to selection (possibly reflecting an improved efficiency of liveweight gain) while, subsequent to the selection age, the percentage of fat in the carcass has typically increased (Malik, 1984).

Subjective observations of an apparent difference in litter size between the high and low IGF-1 lines led to a study of their reproductive performance by Kroonsberg et al (1989). Number of foetuses, average weight per foetus, placental weight, and mammary gland weight were all found to be greater in the high line. However, after accounting for liveweight, only foetal and placental weights remained significantly greater. Whether this difference occurs because of higher levels of IGF-1 in the dam's blood or whether it is a direct effect of the foetus' own IGF-1 system is yet to be determined. The separation of maternal and direct effects will require embryo transfer techniques to be employed. This experiment is currently being planned.

Because of the substantial contribution of the liver to circulating levels of IGF-1 (D'Ercole et al, 1984), and because differences in organ size had been reported in mice transgenic for human GH (Shea et al. 1987), a comparative study of the major organs in high and low IGF-1 mice was undertaken (R.A. Siddiqui and others, unpubl. data). Liver, spleen, heart and kidney weight were all found to be elevated in high line males and females. However, after accounting for liveweight, the liver was found to be proportionately smaller in high line animals. Thus, it would appear that either liver tissue in high line animals produces more IGF-1 per unit weight or IGF-1 has a longer half-life in high line stock.

Furthermore, the possibility that IGF-1 production could have been increased in other organs and/or tissues cannot be ignored. When comparisons were made at the same liveweight, spleens from high line animals were heavier at 30 days, but by maturity this advantage had disappeared. No function for the spleen in the somatotropic axis has been proposed. However, several authors have noted changes in spleen weight following exogenous GH/IGF-1 administration (Guler et al. 1988; Skottner et al. 1989) and in transgenic mice (Shea et al. 1987; Mathews et al. 1988b). In a preliminary histological study of spleens from high and low line mice, it was found that high line mice had greater proportions of haemopoietic tissue (M.J. Birtles and others, unpubl. data). The significance of these findings is the subject of further study.

Merimee et al (1987) observed that plasma concentrations of IGF-1 in male pygmies showed no elevation at adolescence, while testosterone levels showed the increase expected in males of this age. They hypothesised that circulating IGF-1 was necessary for the pubertal growth spurt seen in male humans without the pygmy condition and that high circulating IGF-1 levels at puberty resulted from the associated rise in testosterone levels. Siddiqui et al (1989) reported a study in which they produced 2 castrated groups and a sham operated group for each of the high and low IGF-1 mouse lines. One of the castrated groups received testosterone replacement therapy immediately and the other at 42 days of age. The sham operated and early testosterone replacement groups grew faster than the third group until 42 days of age. However, IGF-1 levels were not different between any of the 3 treatment groups, within line. Therefore, it would appear that, in males not carrying a major gene for growth deficiency, stimulation of growth by testosterone does not act via circulating IGF-1 levels. Furthermore, the testosterone replacement did not act differentially in the 2 selection lines, suggesting that the difference in growth between males of these lines is not due to differences in sensitivity to androgens.

A further mouse IGF-1 selection experiment has been reported by Baker et al (1989). In their experiment, selection was based on individual plasma IGF-1 concentrations at 84 days of age. Lines were replicated once with 8 pairs being maintained for each of the high, control and low lines. Equivalent lines were also maintained for 84 day liveweight. Baker et al (1989) reported realised heritabilities of 0.10 ± .01 and 0.41 ± .10 for IGF-1 levels and liveweight, respectively, and a realised genetic correlation of 0.54 ± .02 after 5 generations of selection. Furthermore, selection for high 84 day IGF-1 levels increased relative weights of lean tissue and bone and increased litter size at birth. These results are generally consistent with those reported by Blair et al (1989), Kroonsberg et al (1989) and Siddiqui et al (1990). However, there is a necessity to establish the function of circulating IGF-1 in animals of different ages. Once these functions are known, animal breeders will be better able to choose the optimum time for selection to meet the objective of increased efficiency of lean growth.

Sheep

Following the encouraging results from the Massey University mouse IGF-1 selection experiment, a selection experiment was established using Romney sheep. In January 1987, three groups of four 5 month-old rams were chosen based on either high, low or average IGF-1 levels. Blood samples for IGF-1 determination were collected by jugular venipuncture from 111 twin-born rams 12 hours off pasture. To establish the ewe flocks, 300 mixed-age commercial Romney ewes were purchased and randomly assigned to the high, control or low lines (100 per line). The selected rams were first mated in March 1988 at 18 months of age, and then used again in March 1989 at 30 months of age. The IGF-1 levels and liveweights of the first generation of selected animals are shown in Table 2. The IGF-1 levels appear to have separated between the high and low lines but the control line is similar to the low line. The selection differential generated between the high and low line rams was 293 ng/ml. After allowing for no selection in the females, the 26 ng/ml difference in the first generation progeny corresponds to a realized heritability of .18 ± .15. This value is similar to those reported from the mouse selection experiments of Blair et al (1989) and Baker et al (1989). There were no apparent differences in growth.

In conclusion, there is good evidence for an involvement of the somatotropic axis in the genetic regulation of growth. Among the components of this axis, IGF-1 holds promise as a physiological indicator of genetic merit for growth. Based on present evidence, primarily from laboratory species, selection for increased IGF-1 levels is likely to result in enhanced growth rates, increased mature body size, improved reproductive performance and little change in body composition at a given weight. Since IGF-1 is measurable in both sexes at a young age, it would seem a potentially useful trait to use as an indirect physiological predictor of growth. However, additional work with farm species (such as our sheep IGF-1 selection experiment) is required to confirm this optimism.

Table 2 Least squares means (± se) for IGF-1 levels and liveweights by sex or selection line for the first generation of offspring in a sheep IGF-1 selection experiment

	Sex		Line		
	Male	Female	High	Control	Low
IGF-1 (ng/ml)	415 ± 11.9	421 ± 9.3	372 ± 10.6	339 ± 11.0	346 ± 10.8
12 wk weight (kg)	21.1 ± .3	19.2 ± .3	20.2 ± .3	19.4 ± .3	20.8 ± .3
16 wk weight (kg)	23.6 ± .3	21.5 ± .3	22.6 ± .4	21.6 ± .4	23.4 ± .4
26 wk weight (kg)	-	28.0 ± .4	28.4 ± .6	26.3 ± .7	28.7 ± .7

REFERENCES

BAKER, R.L., BASS, J.J. et al. 1989. Proc. Endo. Soc. Aust. and N.Z. Soc. Endo. 32: 127 (abstract).

BAUMAN, D.E. and McCUTCHEON, S.N. 1986. In: Control of Digestion and Metabolism in Ruminants. Eds. L.P. Milligan et al. Prentice-Hall, N.J., U.S.A.

BLAIR, H.T., McCUTCHEON, S.N., MACKENZIE, D.D.S., GLUCKMAN, P.D., ORMSBY, J.E. and BREIER, B.H. 1989. Genet. Res. 53: 187-191.

BRADFORD, G.E. and FAMULA, T.R. 1984. Genet. Res. 44: 293-308.

BREM, G., MULLER, M., BRENIG, B., SPRINGMANN, K., KRAUBLICH, H. and WINNACKER, E-L. 1988. In: Control and Regulation of Animal Growth. EAAP Publ. No. 36, Pp 75-84.

BUONOMO, F.C., LAUTERIO, T.J., BAILE, C.A. and CAMPION, D.R. 1987. Dom. Anim. Endo. 4: 23-31.

CARTER, M.L., McCUTCHEON, S.N. and PURCHAS, R.W. 1989. N.Z. J. Agric. Res. 32: 343-353.

CASCIERE, M.A., HAYES, N.S., KELDER, B., KOPCHICK, J.J., CHICCHI, G.G., SLATER, E.E. and BAYNE, M.L. 1988. Endo. 122: 1314-1320.

CHARLTON, H.M. 1984. Q.J. Exptl. Physiol. 69: 655-676.

D'ERCOLE, A.J., STILES, A.D. and UNDERWOOD, L.E. 1984. Proc. Natl. Acad. Sci. 81: 935-939.

EIGENMANN, J.E., AMADOR, A. and PATTERSON, D.F. 1988. Acta. Endo. 118: 105-108.

EIGENMANN, J.E., ZANESCO, S., ARNOLD, U. and FROESCH, E.R. 1984a. Acta Endo. 105: 289-293.

EIGENMANN, J.E., PATTERSON, D.F. and FROESCH, E.R. 1984b. Acta Endo. 106: 448-453.

GEFFNER, M.E., GOLDE, D.W., LIPPE, B.M., KAPLAN, S.A., BERSCH, N. and LI, C.H. 1987. J. Clin. Endo. Metab. 64: 1042-1046.

GLUCKMAN, P.D., BREIER, B.H. and DAVIS, S.R. 1987. J. Dairy Sci. 70: 442-466.

GULER, H-P., ZAPF, J., SCHEIWILLER, E. and FROESCH, E.R. 1988. Proc. Natl. Acad. Sci. 85: 4889-4893.

HAMMER, R.E., BRINSTER, R.L., ROSENFELD, M.G., EVANS, R.M. and MAYOR, K.E. 1985a. Nature 315: 413-416.

HAMMER, R.E., PURSEL, V.G., REXROAD, C.E., WALL, R.J., BOLT, D.J., EBERT, K.M., PALMITER, R.D. and BRINSTER, R.L. (1985b). Nature 315: 680-683.

HOLDER, A.T., WALLIS, M., BIGGS, P. and PREECE, M.A. 1980. J. Edo. 85: 35-48.
HUYBRECHTS, L.M., KING, D.B., LAUTERIO, T.J., MARSH, J. and SCANES, C.G. 1985. J. Endo. 104: 233-239.
KROONSBERG, C., McCUTCHEON, S.N., SIDDIQUI, R.A., MACKENZIE, D.D.S., BLAIR, H.T., ORMSBY, J.E., BREIER, B.H. and GLUCKMAN, P.D. 1989. J. Reprod. Fert. 87: 349-353.
LARON, Z., KLINGER, B., ERSTER, B. and SILBERGELD, A. 1989. Acta Endo. 121: 603-608.
LAUTERIC, T.J., TRIVEDI, B., KAPADIA, M. and DAUGHADAY, W.J. 1988. Comp. Biochem. Physiol. 91A: 15-19.
MALIK, R.C. 1984. J. Anim. Sci. 58: 577-590.
MATHEWS, L.S., HAMMER, R.E., BRINSTER, R.L. and PALMITER, R.D. 1988a. Endo. 123: 433-437.
MATHEWS, L.S., HAMMER, R.E. BEHRINGER, R.R., D'ERCOLE, A.J., BELL, G.I., BRINSTER, R.L. and PALMITER, R.D. 1988b. Endo. 123: 2827-2833.
MERIMEE, T.J., ZAPF, J., HEWLETT, B. and CAVALLI-SFORZA, L.L. 1987. New Eng. J. Med. 316: 906-911.
NORTON, S.A., ZAVY, M.T., MAXWELL, C.V., BUCHANAN, D.S. and BREAZILE, J.E. 1989. Am. J. Physiol. 257: E554-560.
OLSON, K.C., FENN, J., et al. 1981. Nature 293: 408-411.
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: 611-615.
PURSEL, W.G., PINKERT, C.A., MILLER, K.F., BOLT, D.J., CAMPBELL, R.G., PALMITER, R.D., BRINSTER, R.L. and HAMMER, R.E. 1989. Science 244: 1281-1288.
RINGBERG-LUND-LARSEN, T. and BAKKE, H. 1975. Acta Agric. Scand. 25: 231-234.
ROBERTS, C.A., McCUTCHEON, S.N., BLAIR, H.T., GLUCKMAN, P.D. and BREIER, B.H. 1990. Dom. Anim. Endo. (in press).
ROBERTSON, A. 1987. In: Research in Cattle Production Danish Status and Perspectives in Honour of A. Neimann-Sorensen. Held 1 May 1987 in Copenhagen, Denmark, Pp 219-226.
SCANES, C.G., MARSH, J., DECUYPERE, E. and RUDAS, P. 1983. J. Endo. 97: 127-135.
SHEA, B.T., HAMMER, R.E. and BRINSTER, R.L. 1987. Endo. 121: 1924-1930.
SIDDIQUI, R.A., BLAIR, H.T., McCUTCHEON, S.N., MACKENZIE, D.D.S., GLUCKMAN, P.D. and BREIER, B.H. 1990. J. Endo. 124: 151-158.
SIDDIQUI, R.A., McCUTCHEON, S.N., MACKENZIE, D.D.S., BLAIR, H.T., ORMSBY, J.E., GLUCKMAN, P.D. and BREIER, B.H. 1989. Acta. Endo. 121: 686-690.
SIMM, G., YOUNG, M.J. and BEATSON, P.R. 1987. An. Prod. 45: 465-475.
SKOTTNER, A., CLARK, R.G., FRYKLUND, L. and ROBINSON, I.C.A.F. 1989. Endo. 124: 2519-2526.
SMITH, C. 1986. An. Prod. 42: 81-88.
TIXIER-BOICHARD, M., HUYBRECHTS, L.M., KUHN, E., DECUYPERE, E., CHARRIER, J. and MONGIN, P. 1989. Genet. Sel. Evol. 21: 217-234.
VIZE, P.D., MICHALSKA, A.E., ASHMAN, R., LLOYD, B., STONE, B.A., QUINN, P., WELLS, J.R.E. and SEAMARK, R.F. 1988. J. Cell Sci. 90: 295-300.
WARD, K.A., MURRAY, J.D., SHANAHAN, C.M., RIGBY, N.W. and NANCARROW, C.D. 1989. In: The Biology of Wool and Hair. Chapman and Hall, Pp 465-477.
WILLEBERG, P., KASTRUP, K.W. and ANDRESEN, E. 1975. Nord. Vet. Med. 27: 448-454.