

USING JUVENILE IGF-I MEASURES IN PIG BREEDING PROGRAMS

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Background

Insulin-like growth factor-I (IGF-I) is a naturally occurring polypeptide produced in the liver, muscle and fat tissues (Hossner et al. 1997). Circulating IGF-I is usually bound with one of six binding proteins (BPs), which act to control the distribution, function and activity of IGF-I in animals. IGF-I has several roles in growth and development during the post-natal growth period, although typically it's association with growth hormone takes precedence in the literature. IGF-I mediates the effects of growth hormone (GH); has localised effects on the tissues of production; and acts as an insulin-like metabolic regulator (Hossner et al. 1997). Overall, IGFs (IGF-I and IGF-II) form part of a very complex system, many aspects of which are not completely understood.

The concentration of circulating IGF-I can be measured relatively easily in blood plasma. However, BPs must first be stripped from the IGF-I molecules, and procedures used should be validated for the application investigated. For example, extraction methods to remove binding proteins differ in their suitability according to the types and relative concentrations of binding proteins present (see Holly and Hughes, 1994), which are known to change with age.

Historical use of IGF-I in selection experiments

As a result of its endocrine role and the relative stability of circulating levels, IGF-I was historically used as a substitute for measuring growth hormone. Serum concentrations of IGF-I are heritable and associated with a number of growth characteristics in various species. However, expected correlated responses in economically important traits have not always occurred under selection for IGF-I measured this way in growing animals (reviewed by Hossner et al. 1997).

An incomplete understanding of IGF-I function at the endocrine level, and/or under different physiological states has, amongst other factors, probably contributed towards the variable results observed from selection experiments. Phenotypic correlations between IGF-I concentrations measured in juvenile versus growing animals are generally low (eg. Lamberson et al., 1995) demonstrating that IGF-I is not very repeatable when recorded on the same animal at different ages. In addition to age related changes, circulating IGF-I levels are also influenced by external factors such as nutrition, season, and sex. These effects need to be accounted for in the selection process, or the accuracy of selection and predictability of

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correlated responses will be reduced. Further, assay procedures can be complicated by the presence of binding proteins, which are known to vary with age (Harrell et al. 1999). Thus, some assay procedures can potentially give rise to an age related bias in values for IGF-I concentrations. Rates of IGF-I secretion and clearance also change during adaptation to stress (Hossner et al. 1997).

In fact, Owens et al. (1997) and de Greef et al. (2000) argued that IGF-I levels recorded in growing pigs (ie 30+ kg) were more indicative of current growth status than the potential for future performance. In contrast, the approach of Luxford et al. (1998) was to measure IGF-I levels in juvenile piglets shortly after weaning (~25 to 35 days of age). This testing procedure coincided with the piglet's recovery from the stresses of weaning, during a period of mobilisation of fat reserves, and where synthesis of IGF-I should start increasing (Hossner et al. 1997). Further, there is evidence that in the young piglet the IGF-I/GH axis is not mature. For example, Harrell et al. (1999) demonstrated that consistent and significant increases in IGF-I levels following challenges with exogenous porcine somatotropin (pST) only occur after 37 days of age, thereafter increasing with age. Thus, differences between juveniles in circulating IGF-I concentrations are less likely to be due to differences in nutrition, GH levels, and other hormonally mediated effects (eg. sex effects), and may reflect other causes of variation between individuals. Despite this standardisation, corrections for some systematic effects (eg age, sex, seasonal assay effects, and the interval from weaning to bleeding) are often still required.

Use of juvenile IGF-I in breeding programs

When variation due to the above systematic effects is removed, the concentration of IGF-I circulating in the blood plasma of weaned (juvenile) piglets is genetically correlated with several economically important performance traits (Luxford et al. 1998; Hermesch et al. 2001; Lahti et al. 2001). Consequently, information on juvenile IGF-I concentration can be used as an early physiological indicator of performance traits traditionally measured later in life. This facilitates preselection of which animals to performance test if testing capacity is limited, or if early castration decisions are required. In particular, moderate to high genetic correlations exist between juvenile IGF-I levels and feed conversion ratio (FCR). Thus, where FCR or feed intake are not measured directly, indirect information can be provided by data on juvenile IGF-I levels. Juvenile IGF-I also provides additional information towards the overall breeding objective through genetic correlations with other traits.

The measurement of IGF-I for selection purposes, known as PrimeGRO™ IGF-I, has international patents granted and pending. This article provides a summary of trial results for juvenile measures in pigs, along with information accumulating from other studies.

Summary of Primegro trial results for juvenile IGF-I

Original studies on the relationships between IGF-I and performance traits were conducted at QAF Meat Industries (formerly Bunge Meat Industries, Australia) using populations developed from predominantly Landrace and Large White origins. Since then, there has been extensive testing for juvenile IGF-I and further analyses of different lines within QAF, which include infusions from other breeds. Much smaller trials were also implemented in other populations, both in Australia and overseas. A summary of parameter estimates from several studies is provided in Table 1. Standard errors for parameters are mostly available in Bunter et al. (2002).

Trial results demonstrate that IGF-I concentration measured in juvenile pigs is a moderately heritable measure. Further, genetic correlations indicate that downward selection for juvenile IGF-I should result in favourable correlated responses in backfat (BF) and FCR. Variation between studies in estimated correlations was evident, but the magnitude and/or direction of correlations between traits were generally consistent. Results for growth (lifetime or on test) were more variable, although average values suggest an overall genetic correlation close to zero between growth rate and juvenile IGF-I. Variation between estimates in parameter estimates is attributed to sampling issues (ie small trials) and/or population differences. Relatively few studies were able to record feed intake and FCR directly.

Table 1. Heritability estimates for IGF-I along with genetic correlations between IGF-I and economically important performance traits^A (ne: not estimated)

Study ^B	Heritability		Genetic correlations between IGF-I &			
	IGF-I	ADG	BF	DFI	TDG	FCR
QAF 1 (1996)	0.20	-0.47	0.29	0.37	ne	0.84
QAF 2 (2000)	0.23	0.23	0.46	0.52	-0.53	0.51
QAF 3 (2001)	0.24	0.12	0.46	ne	ne	ne
USA 1 (2001)	0.58	0.36	0.54	0.59	0.05	0.59
USA 2 (2001)	0.44	-0.20	0.49	-0.20	-0.12	0.50
UK 1 (2001)	0.53	0.32	0.81	ne	0.12	ne
UK 2 (2001)	0.42	0.13	0.68	ne	0.13	ne
AUS 1 (2002)	0.28	0.08	0.77	ne	ne	ne
GER 1 (2003)	0.29	-0.03	0.66	0.78	-0.18	0.81
Average	0.36	0.06	0.57	0.41	-0.09	0.65

^A Trait abbreviations: ADG: lifetime average daily gain (g); BF: back fat (mm); DFI: average daily feed intake (kg); TDG: average daily gain during performance test (g); FCR: feed conversion ratio (kg feed: kg gain).

Results generally remained consistent where performance test traits were evaluated over either short or longer test periods (QAF 1 versus USA 1 & 2, UK 1 & 2), under *ad-lib* or restricted feeding regimes (QAF 1 & 3 versus QAF 2), and for early-weaned pigs (USA 1 & 2 studies versus rest) (Table 1). Average phenotypic correlations between juvenile IGF-I and BF or FCR were lower, between 0.21-0.15 respectively, because residual correlations between these two traits, which are measured at very different points in time, were generally close to zero. Nevertheless, they illustrate that animals with lower juvenile IGF-I levels should be more efficient and leaner at the end of performance testing, supporting the estimates of genetic correlations. In contrast, studies measuring IGF-I at a later age, closer to the performance-testing period, may show stronger associations between circulating levels and performance measures because environmental conditions affecting values for both traits are more similar. However, some of these studies then fail to demonstrate any genetic association between these IGF-I levels and performance, and/or a predictive capacity of the IGF-I levels for future performance.

Evidence is accumulating for a positive relationship between IGF-I and fat deposition in various physiological studies. Stimulation of cultured porcine preadipocytes with IGF-I in physiological concentrations has been demonstrated to increase the number and size of fat cell clusters (Chen et al. 1995) and their ability to accumulate lipids (Boone et al. 2000). In live

pigs, co-administration of IGF-I with porcine growth hormone reduces the ability of GH to increase gain while suppressing backfat (Klindt et al. 1998). Further, studies in several species suggest IGF-I has a role in providing negative feedback at the hypothalamus and/or pituitary for growth hormone production (eg. for pigs, see Dunaiski et al., 1997). These results suggest that high levels of IGF-I pre-dispose pigs towards increased fat accretion and less efficient lean meat growth. The genetic correlations between IGF-I and lean meat % (r_g : -0.26 ± 0.26 , QAF 1) and scanned eye muscle depth (r_g : -0.21 ± 0.14 , QAF 3) further support the relationship between juvenile IGF-I and lean growth potential, although standard errors for these trait combinations are large.

Hermesch et al. (2001) discuss indirect evidence for the association between IGF-I and efficient lean meat growth. Herpin et al. (1993) had previously noted that selection for lean tissue growth had effects on body and tissue composition, metabolic and hormonal state, and fat metabolism, leading to heavier pigs at birth. Parameter estimates from the large-scale study by Hermesch et al. (2001) were consistent with these observations. Estimates of genetic correlations between juvenile IGF-I or BF and piglet birth weight were both negative (-0.33 ± 0.19 and -0.43 ± 0.17) indicating that genetically leaner pigs have heavier weights at birth and lower levels of juvenile IGF-I.

Recent selection lines in pigs

Cameron et al. (2003) performance tested 342 descendents of six selection lines and a control line, recording IGF-I levels at 6 weeks, 30 kg, 90 kg and at 90kg after fasting. Phenotypic correlations between 6-week and later measures of IGF-I were again low (<0.30), supporting the need to identify age at measurement for IGF-I measures. Within line phenotypic correlations (r_p) between 6-week IGF-I and performance traits were -0.05 (ADG), 0.07 (DFI), 0.10 (FCR), 0.20 (BF) and -0.13 (muscle depth: MD), which were very consistent with corresponding averages (not presented) from the larger trials summarised in Table 1. However, the data of Cameron et al. (2003) were inadequate for estimating genetic parameters, as was identified by the authors. Consequently, between line differences only were used to draw conclusions regarding genetic associations between performance measures and IGF-I levels. Expected between line differences in the 6-week IGF-I (based on genetic correlations) were only observed for the daily feed intake selection lines. With few animals per selection line, the power to detect such genetic associations was relatively limited.

The study of Suzuki et al. (2004) reported correlated responses in IGF-I levels from a Duroc line in Japan, selected under a breeding goal that increased fat levels (see Suzuki et al. 2002). This study used data from 832 pigs measured for IGF-I at 8-weeks of age (from generation 4 onwards only). Back fat and intra-muscular fat levels increased under selection at both the genetic and phenotypic levels from generation four onwards. Thus, expected phenotypic trends for IGF-I are positive (from trial results), and this was indeed the case. Despite this, the authors failed to report a significant positive genetic correlation between IGF-I and BF levels (r_g : 0.13 ± 0.08) although the genetic correlation between IGF-I at 8 weeks and intramuscular fat content was significant (0.32 ± 0.10). The study was limited by relatively small sample sizes, the absence of a control line (ie no environmental corrections possible), combined with the estimation of within discrete generation correlations, complicating the interpretation of results. Standard errors were large and pigs were also much older than is recommended for testing under PrimeGROTM IGF-I.

A study is currently underway at Iowa State University that includes IGF-I testing of young animals in a Yorkshire line selected solely for improved residual feed intake (RFI). The objectives of this study are to evaluate the phenotypic and genetic associations between IGF-I and economically important traits associated with growth, composition, and feed intake, in a significant experimental resource population with extensive performance recording for these traits. Correlated responses in juvenile IGF-I concentration to selection for RFI will be demonstrated when this study is completed (contact: Jack Dekkers).

Studies in cattle

IGF-I is a protein with structure and functions very well conserved across a range of species. Consequently, it might be expected that genetic relationships between IGF-I and performance traits will be similar in other livestock species, for comparable traits, to those estimated for pigs.

There are now several studies available for cattle. Australian studies generally confirm moderate heritabilities (~0.30) for IGF-I levels measured at or close to weaning; moderate to high genetic correlations between subcutaneous (0.2-0.6) or intra-muscular (0.2-0.5) fat measures and IGF-I; and moderate to high genetic correlations (0.31-0.63) between IGF-I and net (or residual) feed intake (NFI) in *Bos taurus* and *Bos indicus* cattle breeds (Johnston et al., 2002; Moore et al., 2004). Results from earlier studies in experimental herds (Johnston et al., 2002) are well supported by much larger scale Industry seedstock herd data (N~6000 records for IGF-I in Moore et al., 2004). Further, results from these studies are very consistent with those from the earlier pig research. That is, feed efficiency in beef cattle should be improved indirectly by selecting for lower IGF-I. Further Australian studies are underway to: confirm the repeatability of IGF-I measures taken at different ages; to estimate parameters for IGF-I under different feeding regimes, in *Bos indicus* cattle breeds, or with new traits (eg meat quality); and to improve accuracy of existing parameter estimates between IGF-I and traits like NFI. Testing at weaning was partially motivated by the Australian studies in pigs where it was established that the associations between IGF-I and performance traits varied with the age at testing. However, in both species, testing close to weaning also generally suits typical management practices.

In contrast, American researchers have focussed on IGF-I measures taken post-weaning, during performance testing under feedlot conditions. Davis and Simmen (1997) originally reported negative genetic correlations between post-weaning IGF-I and weaning or post-weaning weights and gain, suggesting downwards selection for IGF-I would benefit these traits. Moore et al. (2004) later confirmed negative estimates of genetic correlations between IGF-I and 200 or 400 day weights in a much larger data set. Using a limited number of records (~450) for carcass traits, Davis and Simmen (2000) also reported negligible genetic correlations between hot carcass weight and IGF-I, and moderate negative correlations between IGF-I and backfat thickness, marbling score, and quality or yield grades. Thus, results for weights were not consistent between the 1997 and 2000 papers. Davis et al. (2003) later concluded that the associations between IGF-I and fat thickness or muscling recorded using ultra-sound during the post-weaning feedlot period were not strong when data were adjusted to a constant weight. However, genetic and phenotypic correlations between mean IGF-I and back fat thickness, corrected to a constant age, at the end of performance testing were moderate and positive (0.19-0.30). The direction of this correlation was inconsistent with results from the 2000 paper, again possibly reflecting relatively low (~640) record

numbers. However, the latter results are more consistent with the parameter estimates obtained between IGF-I and fat measures in Australian studies for pigs and cattle, observed in both experimental and seed stock herds.

Overall, in American studies, reported parameters relating to back fat thickness have varied between studies for the same reference population (high and low IGF-I selection lines), albeit with differing amounts of data and different trait definitions. Such inconsistencies reflect the relatively low record numbers available for performance traits within experimental selection lines, differences in the modelling strategies employed, and possibly the use of IGF-I measures taken on animals while fed under feedlot conditions. In any case, standard errors of estimates (not reported) would be expected to be large. Possible population differences between American and Australian cattle (resulting in a reversing in the direction of some genetic correlations, eg between IGF-I and fat measures) seem less likely given the strong consistency of results observed across species in the larger Australian data sets.

Conclusions

There is accumulating evidence from several studies involving both pigs and cattle that the concentration of circulating IGF-I is heritable and provides information towards correlated traits included in breeding objectives. In these species, timing of the testing procedure seems important, given that IGF-I levels are affected by the physiological status of animals. In larger commercial populations already undergoing selection focussed on efficient lean meat growth, and with extensive performance recording for both IGF-I and economically important traits, estimates of genetic correlations between IGF-I and fat or efficiency measures appear consistently moderate to high and positive for both pigs and cattle. That is, lower IGF-I levels are associated with leaner more efficient animals.

The very small scale of some trials, and also typically selection lines, has given rise to variable results in the literature. Population differences may also be relevant. However, generally consistent results across at least two farmed species from analyses involving the larger data sets seem supported by conclusions from unrelated physiological studies.

Fine tuning appropriate testing ages and/or physiological states may assist in resolving some apparently conflicting conclusions in the literature as to the information provided by IGF-I testing. It is important to note that Primegro trials have consistently used the same commercially available and validated assay procedures throughout their trials. Further, the Primegro test for pig breeding purposes relies upon:

1. testing at an early age (before 35-42 days of age) and a minimum of 3-5 days after weaning
2. consistent management of weaners pre-testing and/or appropriate modelling to allow for the effects of changes in management on IGF-I levels
3. correction of records for applicable systematic effects (eg age, sex, contemporary group and assay effects)

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References

A list of references can be obtained directly from the author. Email: kbunter2@pobox.une.edu.au..