IGF-1 CONCENTRATION MEASURED IN JUVENILE PIGS PROVIDES INFORMATION FOR BREEDING PROGRAMS: A MINI REVIEW

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BACKGROUND
Insulin-like growth factor-1 (IGF-1) is a naturally occurring polypeptide produced in the liver, muscle and fat tissues (Hossner \textit{et al.}, 1997). IGF-1 has multiple effects on animal growth and metabolism. Original studies focussed on its endocrine role, where IGF-1 interacts with and influences the effects of growth hormone (GH). However, IGF-1 also has autocrine and paracrine functions in or close to tissues of synthesis (Hossner \textit{et al.}, 1997). The cellular level production and functions are probably more significant than endocrine functions prior to maturation of the IGF-1/GH axis (Harrell \textit{et al.}, 1999).

Circulating IGF-1 is usually bound with one of six specific binding proteins (BPs). Binding proteins control the distribution, function and activity of IGF-1 \textit{in vivo} and are produced and expressed in at least one form in almost all tissues. It is thought that mechanisms controlling the expression of BPs during various physiological states (as yet largely undefined) will determine whether IGFs (both IGF-1 and IGF-2) have stimulatory or inhibitory effects on IGF-mediated growth (Hossner \textit{et al.}, 1997). The total concentration of circulating IGF-1 can be measured relatively easily in blood plasma with appropriate assays that first strip the BPs from IGF-1. In the absence of stress and due to the presence of BPs, the total pool of circulating IGF-1 is relatively stable (Hossner \textit{et al.}, 1997).

HISTORICAL USE OF IGF-1 IN SELECTION EXPERIMENTS
As a result of its endocrine role and the relative stability of circulating levels, IGF-1 was historically used as a substitute for measuring GH in growing animals. Serum concentrations of IGF-1 are generally heritable and associated with a number of growth characteristics in various species, and these characteristics have motivated evaluation of IGF-1 as a selection tool. However, correlated responses in economically important traits have not always occurred under selection for IGF-1 measured in growing animals (see review by Hossner \textit{et al.}, 1997).

An incomplete understanding of IGF-1 function at the endocrine level, or under different physiological states, has probably contributed towards the variable results observed from previous selection experiments. For example, relatively low phenotypic correlations between IGF-1 concentrations measured in juvenile versus growing animals ($r_p$: 0.14 and 0.23 between IGF-1 measured at 6 weeks and 30 or 90 kg, Neil Cameron, 2000, pers. comm.) suggests that IGF-1 is not the same trait when recorded at different ages. However, there are no corresponding estimates of genetic correlations to support this contention. Owens \textit{et al.}, (1997)
and de Greef et al. (2000) argue that IGF-1 levels recorded in growing pigs are more indicative of current growth status than the potential for future performance. IGF-1 levels are further influenced by external factors such as nutrition, season, sex and age at measurement, which would reduce the accuracy of selection and predictability of correlated responses if not accounted for in the selection process. Rates of IGF-1 secretion and clearance also change during adaptation to stress (Hossner et al., 1997). Further, assay procedures can be complicated by the presence of BPs, more or less so depending on the predominant BPs at the time of testing, which are known to vary with age (Harrell et al., 1999).

A more recent approach (Luxford et al., 1998) has been that of measuring IGF-1 levels in juvenile piglets shortly after weaning (~25 to 35 days of age). The timing of testing coincides with the piglet’s recovery from the stresses of weaning, during a period of mobilisation of fat reserves, and where synthesis of IGF-1 should be increasing (Hossner et al., 1997). Further, there is evidence that in the young piglet, the IGF-1/GH axis is not mature at this age (Harrell et al., 1999). Thus, circulating IGF-1 concentrations are less likely to be affected by changes in nutrition, GH levels, and other hormonally mediated effects (eg. sex effects).

USE OF JUVENILE IGF-1 IN BREEDING PROGRAMS

The concentration of IGF-1 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-1 concentration can be used as an early physiological indicator of performance traits traditionally measured later in life, and also facilitates preselection of which animals to performance test if testing capacity is limited, or if early castration decisions are required. Specifically, moderate to high genetic correlations between IGF-1 levels and feed conversion ratio (FCR) point towards its use as an indirect alternative to the direct measurement of FCR. Additional information towards the breeding objective is also generated through genetic correlations between IGF-1 and other traits.

The test used to measure juvenile IGF-1 is now patented as PrimeGRO™ IGF-1, and is available commercially in Australia and overseas. The objective of this paper is to provide a summary of trial results for juvenile measures, along with information accumulating from other studies.

SUMMARY OF TRIAL RESULTS FOR JUVENILE IGF-1

Original studies on the relationships between IGF-1 and performance traits were conducted by Bunge Meat Industries (BMI, Australia) using populations developed from predominantly Landrace and Large White origins. The age at testing for IGF-1 concentration was considerably younger (around 4 - 5 weeks) than that routinely investigated in other scientific studies. Good results motivated extensive testing for juvenile IGF-1 and further analyses of different lines within BMI that included infusions from other breeds. Small trials were also implemented in other populations. Increasing the genetic diversity of populations studied and/or the management systems under which animals are performance tested provides more robust evidence for results observed in the original study.
A summary of results from several studies is provided in Table 1. After appropriate editing for outliers and recording errors, parameter estimates in all studies were obtained using Restricted Maximum Likelihood (REML) methodology. IGF-1 concentration measured in juvenile pigs is a moderately heritable measure, and downward selection should result in favourable correlated responses in backfat (BF) and FCR. Common litter effects inflated heritability estimates in USA and UK studies, but fitting this effect did not significantly alter estimates of genetic correlations. Moreover, results generally remain consistent where performance test traits are evaluated over either short or longer test periods (BMI 1 versus USA 1 & 2, UK 1 & 2), under ad-lib or restricted feeding regimes (BMI 1 & 3 versus BMI 2), and for early-weaned pigs (USA 1 & 2 studies versus rest). The similarity (in terms of direction and magnitude) of parameter estimates across more diverse pig populations and production systems suggests that earlier conclusions are unlikely to be specific to the BMI populations of pigs, although the value of estimated correlations varies between studies.

Table 1. Heritability estimates for IGF-1 along with genetic correlations between IGF-1 and economically important performance traits

<table>
<thead>
<tr>
<th>Study</th>
<th>Heritability</th>
<th>Genetic correlations between IGF-1 &amp;</th>
<th></th>
<th></th>
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</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>IGF-1</td>
<td>ADG</td>
<td>BF</td>
<td>DFI</td>
<td>TDG</td>
<td>FCR</td>
</tr>
<tr>
<td>BMI 1 (1996)</td>
<td>0.20 (.09)</td>
<td>-0.47 (.38)</td>
<td>0.29 (.23)</td>
<td>0.37 (.31)</td>
<td>ne</td>
<td>0.84 (.37)</td>
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<tr>
<td>BMI 2 (2000)</td>
<td>0.23 (.02)</td>
<td>0.23 (.04)</td>
<td>0.46 (.04)</td>
<td>0.52 (.16)</td>
<td>-0.53 (.10)</td>
<td>0.51 (.08)</td>
</tr>
<tr>
<td>BMI 3 (2001)</td>
<td>0.24 (.03)</td>
<td>0.12 (.12)</td>
<td>0.46 (.08)</td>
<td>ne</td>
<td>ne</td>
<td>ne</td>
</tr>
<tr>
<td>USA 1 (2001)</td>
<td>0.58 (.13)</td>
<td>0.36 (.17)</td>
<td>0.54 (.14)</td>
<td>0.59 (.27)</td>
<td>0.05 (.19)</td>
<td>0.59 (.40)</td>
</tr>
<tr>
<td>USA 2 (2001)</td>
<td>0.44 (.12)</td>
<td>-0.20 (.17)</td>
<td>0.49 (.15)</td>
<td>-0.20 (.38)</td>
<td>-0.12 (.18)</td>
<td>0.50 (.38)</td>
</tr>
<tr>
<td>UK 1 (2001)</td>
<td>0.53 (.29)</td>
<td>0.32 (.22)</td>
<td>0.81 (.32)</td>
<td>ne</td>
<td>0.12 (.27)</td>
<td>ne</td>
</tr>
<tr>
<td>UK 2 (2001)</td>
<td>0.42 (.27)</td>
<td>0.13 (.22)</td>
<td>0.68 (.15)</td>
<td>ne</td>
<td>0.13 (.22)</td>
<td>ne</td>
</tr>
<tr>
<td>Pooled^c Estimates (including and excluding estimates from restricted feeding data)</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>including</td>
<td>0.28</td>
<td>0.15</td>
<td>0.50</td>
<td>0.39</td>
<td>-0.16</td>
<td>0.56</td>
</tr>
<tr>
<td>excluding</td>
<td>0.32</td>
<td>0.09</td>
<td>0.52</td>
<td>0.30</td>
<td>0.03</td>
<td>0.65</td>
</tr>
</tbody>
</table>

^a Trait abbreviations: ADG: lifetime average daily gain (g); BF: back fat at the P2 site (mm); DFI: average daily feed intake (kg); TDG: average daily gain during performance test (g); FCR: feed conversion ratio (kg feed: kg gain).

^b BMI 1: Lines 1 & 2 (LW and LR based) – individually penned boars, short late test (between 18-22 weeks of age), fed ad-lib (No. records for IGF-1: N=1551).

BMI 2: Lines 5, 7 & 8 (synthetics of LW, LR, Hampshire and Duroc breeds) – individually penned boars, late test (18-24 weeks), restricted feed (N=15800).

BMI 3: Lines 1, 2 and 7 (LW and LR based) – group pen test (18-24 weeks), fed ad-lib (N=9990).

USA 1: Bell Farms LW - long group test (13-25 weeks) with electronic feeders, fed ad-lib (N=469).

USA 2: Bell Farms LR – long group test (13-25 weeks) with electronic feeders, fed ad-lib (N=540).

UK 1: Rattlerow LW, group pen test (14-22 weeks), no feed intake recorded, fed ad-lib (N=300).

UK 2: Rattlerow LR, group pen test (14-22 weeks), no feed intake recorded, fed ad-lib (N=328).

^c Estimates are weighted by the inverse of their standard error.

Evidence is also accumulating for a positive relationship between IGF-1 and fat deposition in various physiological studies. Stimulation of cultured porcine preadipocytes with physiological
concentrations of IGF-1 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-1 with porcine growth hormone reduces the ability of GH to increase gain while suppressing backfat (Klindt et al., 1998). Thus, high levels of IGF-1 pre-dispose pigs towards increased fat accretion, and consequently less efficient lean meat growth. Genetic correlations between IGF-1 and lean meat % ($r_g$: -0.26 ± 0.26, BMI 1) and scanned eye muscle depth ($r_g$: -0.21 ± 0.14, BMI 3) support the relationship between juvenile IGF-1 and lean growth potential, although standard errors for these trait combinations are large.

Less direct evidence for the association between IGF-1 and efficient lean meat growth is discussed in the paper by Hermesch et al., (2001). Similar patterns of genetic correlations were evident between piglet traits recorded at birth and juvenile IGF-1 or end of test BF. Estimates of genetic correlations between juvenile IGF-1 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-1. Herpin et al., (1993) had previously noted that selection for lean tissue growth appeared to have effects on body and tissue composition, metabolic and hormonal state, and fat metabolism, leading to heavier pigs at birth.

CONCLUSION
There is good evidence that IGF-1 concentration measured in recently weaned juvenile piglets is heritable and provides information towards correlated traits included in the breeding objective of populations focussed on efficient lean meat growth.

REFERENCES