Genetic variation in sperm production

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In boars, the primary determinant of daily sperm production is the number of Sertoli cells, which establishes testicular weight. The only breed comparison of foetal testicular development in boars contrasted two diverse breeds, White composite (WC, Landrace-Yorkshire) with Meishan, a Chinese breed that undergoes pubertal development at a young age and has small testicular size. During the prenatal period, the pattern of change in testicular development is similar in these two breeds with both having their greatest proportion of proliferating Sertoli cells at 90 days of gestation, and with WC boars possessing more Sertoli cells and greater mass of seminiferous tubules during the latter half of gestation. During the first month of life, Meishan boars accumulate Sertoli cells and mass of seminiferous tubules at a greater rate than WC boars, and Meishan boars undergo terminal differentiation of Sertoli cells at a younger age. Postpubertal boars, within each breed and crossbreds of the two breeds, with small testicular size have increased circulating concentrations of follicle-stimulating hormone. No direct breed comparisons of testicular development are apparent for postpubertal boars of other breeds. Accepting the limitations of data reported from different laboratories, Piau boars reach puberty at an older age and have a greater proportion of their testes occupied with seminiferous tubules than Meishan boars; both breeds have small testes. A gene or genes on the X chromosome code for small testicular size in Meishan crossbred boars; genetic determinants of testicular size and sperm production in other breeds remain to be identified.

Introduction

Daily sperm production correlates positively with mature testicular size in boars (Fig. 1; Hemsworth *et al.*, 1983; Huang and Johnson, 1996) and with number of Sertoli cells (Orth *et al.*, 1988; Lunstra *et al.*, 2003). Fixed costs associated with collection of semen from boars are high relative to the modest number of doses of sperm per ejaculate. Consequently, technology that identifies boars with larger testes yielding more doses of sperm per collection reduces the cost of swine production for producers who use artificial insemination. Differences in number of sperm per ejaculate can vary by more than three fold among breeds (Kennedy and Wilkins, 1984; Castro *et al.*, 1991; Borg *et al.*, 1993; Colenbrander *et al.*, 1993) with the greatest daily

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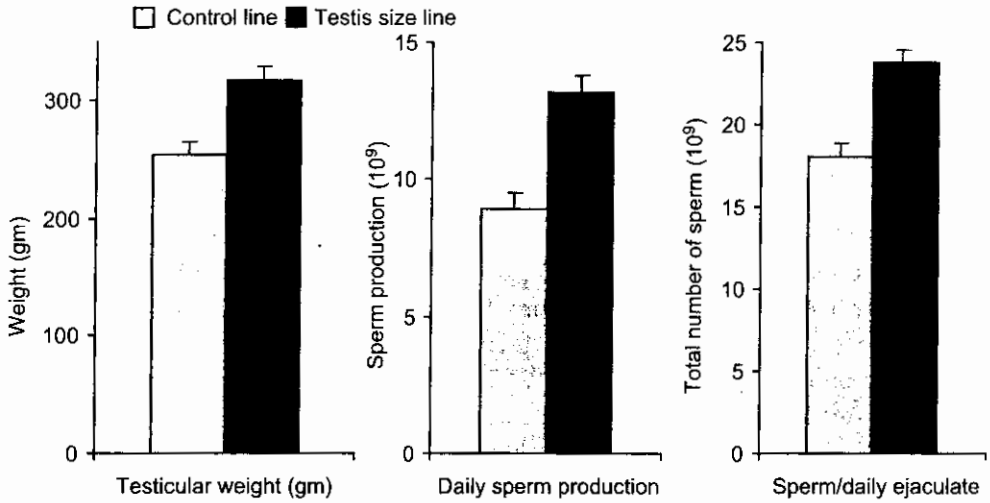

Fig. 1 Sperm production in boars selected for larger testicular size at 150 days of age (n = 24) relative to randomly selected controls (n = 18), adapted from Huang and Johnson (1996); left panel – parenchyma weight of one testicle at ~ 13 months of age; centre panel – daily sperm production for one testicle estimated by determination of homogenisation resistant spermatids; right panel – mean number of sperm per ejaculate during a 3-week period of daily collections just prior to castration.

sperm production in breeds commonly found in intensive swine production. Sperm production improves with age up to two years (Swierstra, 1973; Kennedy and Wilkins, 1984), in response to direct selection for testicular size (Toelle *et al.*, 1984; Johnson *et al.*, 1994) and as a consequence of heterosis (Wilson *et al.*, 1977). However, full understanding of the biological basis for breed differences in sperm production is lacking, although the number of Sertoli cells at completion of puberty is a primary limit. Earlier reviews have summarised endocrine changes associated with testicular development in boars (Colenbrander *et al.*, 1982; Lunstra *et al.*, 1997; Franca *et al.*, 2005). The present assessment of the literature addresses genetic variation in testicular development with emphasis on seminiferous tubules.

Prenatal testicular development

The rate of development of indifferent porcine gonads has not been scrutinised for breed differences. Genetic sex becomes established at conception; the female phenotype develops unless specific signals induce the male phenotype through a cascade of transcriptional regulators at critical stages (Pailhoux *et al.*, 2001; Cupp and Skinner, 2004; Park and Jameson, 2005). In male pigs, primordial germ cells and a population of somatic cells that contribute to gonadal growth migrate from the primitive gut to the sexually indifferent genital ridge beginning after day 18 of gestation (Takagi *et al.*, 1997; McCoard *et al.*, 2001). By day 23, expression of the sex-determining gene, SRY, in males defines initiation of testis formation (Daneau *et al.*, 1996; Parma *et al.*, 1999), but at day 24 embryonic gonads remain morphologically indifferent (Pelliniemi, 1975). However, at day 26, testicular cords that enclose germ cells and functioning Sertoli cells, indicated by production of anti-Mullerian hormone (AMH), become apparent

(Pelliniemi, 1976; Tran *et al.*, 1977; McCoard *et al.*, 2001). Peritubular myoid cells enclose these cords leading to seminiferous tubule formation (Pelliniemi, 1976; McCoard *et al.*, 2001).

The only apparent breed comparison pertaining to prenatal testicular development in boars (McCoard *et al.*, 2002b, 2003b) contrasted Landrace-Yorkshire (White composite, WC) with Meishan, a Chinese breed with small testes that reaches puberty at a much younger age than WC boars (Okwun *et al.*, 1996b; Lunstra *et al.*, 1997). Progression of testicular development in these two diverse breeds followed a remarkably similar pattern; AMH was detected in 40-50% of the males within each breed at 26 days of gestation and in 100% of the boars of both breeds by day 28. Similarly, 17 alpha-hydroxylase/17, 20-lyase cytochrome P450, an indicator of steroid synthesis in Leydig cells, was observed in ~ 50% of boars of each breed at day 28 and in all boars at day 30 of gestation. Between days 30 and 50 of gestation, foetal WC males grew to heavier weights than Meishan males (Hunter *et al.*, 1994; McCoard *et al.*, 2003b), and WC boars had greater testicular weight and mass of seminiferous tubules by 60 days of gestation than did Meishan males (Fig. 2). Tubular mass continued to increase rapidly in both breeds throughout gestation with the final two weeks of gestation characterised by accelerated growth (van Straaten and Wensing, 1977). Number of Sertoli cells was consistently greater in WC than in Meishan foetuses, and the magnitude of this difference was proportional to the difference in mature testicular size of these two very diverse breeds (Okwun *et al.*, 1996b). However, at 90 days of gestation, the largest proportion of Sertoli cells was in a proliferative stage in both breeds, and the number of germ cells did not differ in foetal Meishan and WC boars (McCoard *et al.*, 2003b). The increase in number of germ cells was logarithmic throughout the latter half of gestation as observed previously (van Straaten and Wensing, 1977). Because rate of pubertal development and composition of post-pubertal testes are quite different for Meishan and WC boars, we assume the observed changes in mass of seminiferous tubules and number of Sertoli cells during foetal development relate well to other breeds.

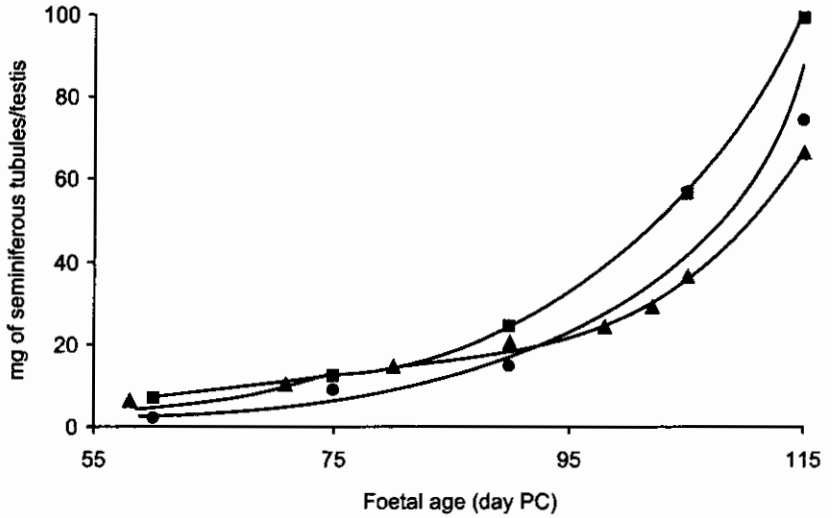

Fig. 2 Estimated weight of the seminiferous tubules within one testicle of foetal boars from three genotypes on specified days postcoitum (PC); day 115 is one-day of age. Data were adapted from McCoard *et al.*, (2003b) for White composite (WC, Landrace x Yorkshire, ■) and Meishan foetuses (●) and from van Straaten and Wensing, (1977) for Dutch Landrace x Yorkshire (L x Y) foetuses (▲).

Postnatal testicular development

Breed differences in postnatal testicular development contrast greatly from the similarity observed in prenatal development of tubular mass. During the first 25 days of postnatal life Meishan boars accumulate Sertoli cells and seminiferous tubules at a more rapid rate than WC boars producing greater mass of tubules despite their lower total testicular weight (Fig. 3; McCoard et al., 2003b). Meishan boars retain this advantage in mass of seminiferous tubules over other investigated breeds for their first 100 days of life (Fig. 4). Rapid accrual of tubular mass, expansion of seminiferous tubule diameter and increasing rate of Sertoli cell accumulation define the onset of early male pubertal development in most mammalian species that have been characterised (Sharpe et al., 2003; Franca et al., 2005).

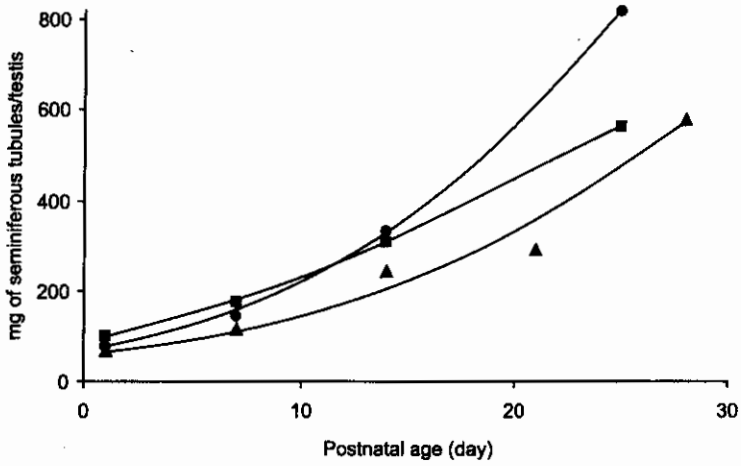

Fig. 3 Estimated weight of the seminiferous tubules within one testicle of boars from three genotypes at specified days of early postnatal age. Data were adapted from McCoard et al., (2003b) for White composite (WC, Landrace x Yorkshire, ■) and Meishan boars (●) and from van Straaten and Wensing (1977) for Dutch Landrace x Yorkshire (L x Y) boars (▲).

An accelerated increase in the diameter of seminiferous tubules distinguishes terminal differentiation of Sertoli cells accompanied with increased secretion and accumulation of fluids as the seminiferous tubules become compartmentalised by tight junctions (Russell and Griswold, 1993; van Haaster et al., 1993). This series of changes signals the ensuing formation of the blood-testis barrier and the first appearance of spermatids indicating onset of puberty (Tran et al., 1981). Functional differences exist between foetal and adult Sertoli cells as they undergo transition from a proliferative stage into fully differentiated cells (Migreene et al., 2003; O'Shaughnessy et al., 2003; Sharpe et al., 2003). Meishan boars undergo pubertal development at a young age (Fig. 4) characterised by increased diameter of seminiferous tubules at 30-45 days of age (Harayama et al., 1991; Lunstra et al., 1997) compared to other breeds which exhibit increased diameter of seminiferous tubules after 100 days of age (van Straaten and Wensing, 1977; Allrich et al., 1983; Lee et al., 1987; Kosco et al., 1989; Franca et al., 2000). Meishan and Piau boars attain similar daily sperm production (Table 1) but achieve this through distinctly different patterns of testicular composition and tubular growth. Data relating to testicular weight and composition of present-day boars were not found. The emphasis on selection for leaner carcasses during the past decades potentially produced a delay in pubertal development as earlier pubertal development was associated with an increase in backfat thickness (Johnson et al., 1994).

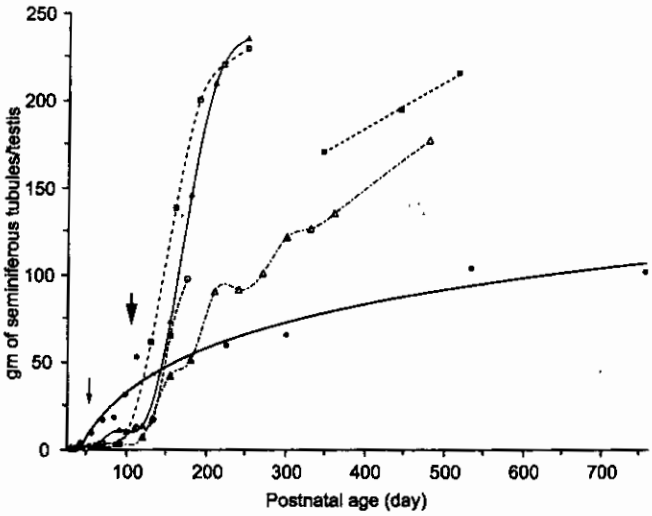

Fig. 4 Estimated weight of the seminiferous tubules within one testicle of boars from six genotypes at specified days of postnatal age. Data were adapted from van Straaten and Wensing (1977) for Dutch Landrace x Yorkshire (L x Y, open circles); from Okwun *et al.*, (1996a and 1996b), Lunstra *et al.*, (1997) and D.D. Lunstra, unpublished, for Meishan (closed circles); from Okwun *et al.*, (1996a and 1996b), Lunstra *et al.*, (1997) and D.D. Lunstra, unpublished for 4-breed White composite (WC, closed squares); from Allrich *et al.*, (1983) for Landrace x Duroc (L x D, open squares); from Castro *et al.*, (1991) and Franca *et al.*, (2000) for Piau (open triangles) and from Lee *et al.*, (1987) for Hampshire x Duroc x Yorkshire (H x D x Y, closed triangles). Small arrow indicates approximate timing of rapid expansion of diameter of seminiferous tubules of Meishan boars, and the large arrow approximates initiation of rapid expansion of diameter of seminiferous tubules in boars of the other five genotypes.

Table 1. Breed differences in testicular composition and sperm production of one testicle

Breed	N	Age (d)	Testicular wt (gm)[5]	Proportion of tubles	TDSP (10^9)[6]	Sperm/day/ gm tubule (10^6)
White Composite[1]	5	346	271	0.69	6.0	35.1
White Composite[2]	13	464	274	0.73	5.5	29.6
Meishan[1]	5	225	135	0.49	2.5	41.5
Meishan[2]	23	525	153	0.57	2.8	34.4
West African[1]	5	332	74	0.60	1.4	35.6
Piau[3]	12	332	159	0.79	2.9	24.2
Piau[3]	3	480	219	0. 81	—	—
Control-White Composite[4]	18	389	286	0.71	8.9	49.1
Select-White Composite[4]	24	409	360	0.71	13.2	58.5

[1]Efficiency of tubules estimated from data of Okwun *et al.*, (1996a, 1996b).
[2]Lunstra *et al.*,(unpublished data adjusted for age within breed; White Composite 297-687 days of age; Meishans 284-889 days of age).
[3]Efficiency of tubules estimated from data of Castro *et al.*, (1991) using daily sperm production as determined by Franca *et al.*, (2000).
[4]Efficiency of tubules estimated from data of Huang and Johnson (1996) using volume percent seminiferous tubules determined by Harder *et al.*, (1995).
[5]Single testis.
[6]Total daily sperm production.

Differences in testicular composition of post-pubertal boars are apparent among breeds, but such differences have not been assessed to any great extent within a standardised evaluation. The volume percentage of seminiferous tubules in testes of post-pubertal boars generally ranges from 65% to 75% in most breeds, but Meishan boars at 55% and Piau boars at 80% characterise the reported extremes (Table 1).

Genetic determinants of tubular mass

In mice, only a few genes have a major impact on testicular weight with a heritability of 0.52 (Chubb, 1992; Zidek *et al.*, 1998). A significant proportion of this variation in testicular size was originally attributed to the Y chromosome (Hunt and Mittwoch, 1987); however, more recent studies determined that specific regions of the X chromosome also significantly impact testicular weight in mice (Elliott *et al.*, 2001; Oka *et al.*, 2004). In boars of a Landrace–Large White composite line, direct selection for larger testes at 150 days of age produced a significant increase in mature testicular weight and an increase in total daily sperm production (Fig. 1; Huang and Johnson, 1996). Moreover, this selection advanced pubertal development based on an earlier increase in the volume percentage of seminiferous tubules and an earlier appearance of tubules with a lumen (Harder *et al.*, 1995). This contrasts with the situation in Meishan and Meishan crossbred boars where larger testicular weights align with later onset of pubertal development (Lunstra *et al.*, 1997; Lunstra *et al.*, 2003). Of particular note in boars selected for greater testicular size, the volume percentage of seminiferous tubules in post-pubertal boars was not affected by selection (Harder *et al.*, 1995), documenting that selection in fact increased both the interstitial and the seminiferous tubular components of the testicles.

The striking difference in mass of seminiferous tubules between Meishan and WC boars (Fig. 4) was exploited by establishing a Meishan crossbred population to further investigate the genetic basis for differences in testicular size. The negative relationship of plasma follicle-stimulating hormone (FSH) concentrations and testicular size provided the initial impetus for interest in these boars (Ford *et al.*, 1997; Lunstra *et al.*, 1997). In crossbred boars (1/2 Meishan x 1/2 WC) that were produced by mating 3/4 Meishan x 1/4 WC sires with 1/4 Meishan x 3/4 WC dams and *vice versa* (Rohrer *et al.*, 2001), it became apparent that post-pubertal plasma FSH concentrations of boars produced by 3/4 Meishan dams were significantly greater than FSH concentrations of boars from 3/4 WC females. Subsequent quantitative trait loci (QTL) analyses determined that testicular size and plasma FSH concentration were associated with a portion of the X chromosome located near the centromere (Rohrer *et al.*, 2001). Post-pubertal boars produced in an ensuing generation confirmed that boars with this region of the X chromosome inherited from the Meishan breed had smaller testes and higher plasma FSH concentrations than boars with this chromosomal region inherited from the WC line (Ford *et al.*, 2001). A subsequent study with Meishan-Duroc crossbred boars castrated at 60 days of age confirmed the QTL for testicular size in this region of the X chromosome (Sato *et al.*, 2003).

In the early studies with Meishan crossbred boars, testicular morphology was evaluated only in boars that represented extremes within the population (Zanella *et al.*, 1999; Lunstra *et al.*, 2003). Boars with high plasma FSH concentrations (the 25% of the population with the smallest testes) mimicked purebred Meishan boars with their low volume percentage and low mass of seminiferous tubules. Similarly, testicular morphology of boars with low plasma FSH concentrations (the 25% with the largest testes) approximated that of WC boars with their greater volume percentage and greater mass of seminiferous tubules. Subsequently, this line of boars was maintained for two additional generations followed by conversion to one-quarter Meishan crossbreds and maintenance for an additional three generations of *inter se* mating. In an evalu-

ation of all boars (1/4 Meishan x 3/4 WC) produced in one farrowing season, testicular weight continued to be 23% heavier in boars with the WC QTL relative to boars with the Meishan QTL. In contrast to previous evaluations, volume percentage of the seminiferous tubules was similar in both groups (54%; Ford *et al.*, unpublished data). Testicular composition approximated that found in Meishan boars in spite of the three-quarter WC background that exists within this population. Thus, this portion of the X chromosome has minimal impact on testicular composition.

Comparative genetic mapping of the porcine X chromosome revealed an order of genes similar, if not identical, to that on the human X chromosome (McCoard *et al.*, 2002a) thereby providing a list of genes as potential candidates to evaluate for polymorphisms that may account for differences in testicular weight (Ross *et al.*, 2005; Harsha *et al.*, 2005). The androgen receptor was an early candidate as its gene resides near the centromere of the X chromosome (Rohrer, 1999), and varying lengths of glutamine and glycine repeats in the open reading frame of androgen receptor are associated with male infertility in humans (Yong *et al.*, 2003; Gottlieb *et al.*, 2005). However, evidence was not found to support variation in the length of these CAG and GGC repeats in the porcine androgen receptor (Song *et al.*, 1999).

The well-characterised extension of Sertoli cell proliferation (i.e., delayed terminal differentiation of these cells) that accompanies hypothyroidism during the early postnatal period in rats and produces larger testes (Hess *et al.*, 1993) directed interest to thyroid-binding globulin (TBG). The gene for this transport protein of thyroxine (T4) resides within the QTL for testicular size in both pigs and mice (McCoard *et al.*, 2002a; Oka *et al.*, 2004). Detection of a polymorphism in the gene for porcine TBG provided an indication that differences in availability of thyroid hormones may regulate testicular size in this species. The Meishan allele codes for a histidine in the binding domain of TBG; whereas the allele that occurs in other investigated breeds of pigs substitutes an alanine for this histidine (Nonneman *et al.*, 2005). This amino acid exchange reduces the binding affinity of TBG for T4 in Meishan pigs relative to the affinity of this protein for T4 in modern-day breeds. At present, this change is associated with differences in testicular size, but additional studies are required to establish that this allelic change is truly responsible for the observed differences.

A second QTL for testicular size was identified on chromosome 3 in prepubertal Meishan-Duroc boars (Sato *et al.*, 2003). This area corresponds closely to QTL for FSH in post-pubertal Meishan-WC boars, but a significant association with testicular weight was not observed in this later study (Rohrer *et al.*, 2001). This may reflect the difference in age at evaluation of testicular weight. At 60 days of age, heavier testicular weights likely relate to earlier terminal differentiation of Sertoli cells and enlargement of the seminiferous tubules in Meishan and Meishan crossbred boars (Lunstra *et al.*,1997; 2003). Collectively, this series of studies clearly documents that mass of the seminiferous tubules is a heritable trait in boars, and as predicted, greater quantities of seminiferous tubules significantly enhanced sperm production. Correspondingly, sperm production in boars has a moderate heritability (Smital *et al.*, 2005).

Efficiency of sperm production

The number of germ cells per Sertoli cell is relatively constant within a species (Russell and Peterson, 1984; Orth *et al.*, 1988). However, the study by Huang and Johnson (1996) observed a 26% increase in mass of seminiferous tubules in boars selected for larger testes which was associated with a 48% increase in total daily sperm production (Table 1). This signifies greater sperm production per unit of tubule (19%) and, if number of Sertoli cells per unit of tubule is constant, sperm production per Sertoli cell increased in boars of the select line. Detailed mor-

phological evaluation of seminiferous tubules in boars from these two lines is required to define composition, but these observations were unexpected due to the assumed constant sperm production per Sertoli cell within a species. Similarly, the initial evaluation of Meishan boars indicated greater production of germ cells per Sertoli cell than observed in WC boars (Okwun *et al.*, 1996a). Further characterisation of Meishan boars based on mass of seminiferous tubules failed to support this difference (Table 1). This issue requires additional investigation as the potential for genetic differences in number of germ cells per Sertoli cell during spermatogenesis would provide a secondary means to improve sperm production of boars.

Endocrine regulation of Sertoli cell proliferation and differentiation

Follicle-stimulating hormone

In vitro and *in vivo* studies with rodents have established the ability of FSH to stimulate proliferation of Sertoli cells during the early postnatal period (Meehan *et al.*, 2000; Allan *et al.*, 2004). In rats, increased proliferation of Sertoli cells with exogenous FSH during early postnatal life produced larger mature testicular size and greater sperm production; however, exogenous FSH treatment was effective only when administered during this specific period (Meachem *et al.*, 1996). Similarly, FSH *in vitro* stimulated proliferation of porcine Sertoli cells isolated from 21-day-old boars (Goddard *et al.*, 2001), and the neonatal and pubertal increases in plasma FSH in Piau boars correlated with periods of rapid accumulation of Sertoli cells (Franca *et al.*, 2000). On the other hand, accumulation of Sertoli cells in Meishan and Meishan crossbred boars are not tightly coupled with changes in plasma FSH concentrations (Ford *et al.*, 2001; Lunstra *et al.*, 2003; McCoard *et al.*, 2003b). Unilateral castration at 1 and 10 days of age increased FSH secretion, but this produced a very modest (~ 16%) increase in number of Sertoli cells in boars that developed large, hypertrophied testes and no increase in number of Sertoli cells in boars that developed small, hypertrophied testes (Ford *et al.*, 2001; Lunstra *et al.*, 2003). As a result, the sensitive period for stimulation of Sertoli cell proliferation in boars apparently does not occur during early postnatal development, leading to the prediction that the coupling of FSH and Sertoli cell accumulation observed by Franca *et al.*, (2000) may be coincidental rather than a cause and effect relationship.

Exogenous FSH administered to boars from 8 to 40 days of age increased the length of seminiferous tubules at 100 days of age (Swanlund *et al.*, 1995). These investigators predicted increased numbers of Sertoli cells in response to exogenous FSH on the assumption that length of seminiferous tubules was proportional to number of Sertoli cells, but they did not directly determine the number of Sertoli cells. Alternative explanations of their findings are that FSH treatment increased the size of existing Sertoli cells as occurs after unilateral castration of boars (Lunstra *et al.*, 2003) or that the increase in number of Sertoli cells was transient as seemingly occurs after unilateral castration of boars (Putra and Blackshaw, 1985). Moreover, there was no association of neonatal (i.e., before 8 weeks of age) concentrations of plasma FSH with mature testicular size in boars (Ford *et al.*, 2001; McCoard *et al.*, 2003b), and boars that will develop large testes accumulate Sertoli cells as plasma FSH declines from days 10 to 56 of age (Fig. 5; Ford *et al.*, 2001; Lunstra *et al.*, 2003). Therefore, we conclude that endogenous FSH during neonatal and prepubertal development of boars is not limiting (i.e. FSH supports proliferation rather than providing a major stimulus to establish number of Sertoli cells present at adulthood). This conclusion questions the applicability of the rodent model of Sertoli cell proliferation to boars, similar to the concern of extending the rodent model to other mammalian species (Walker, 2003).

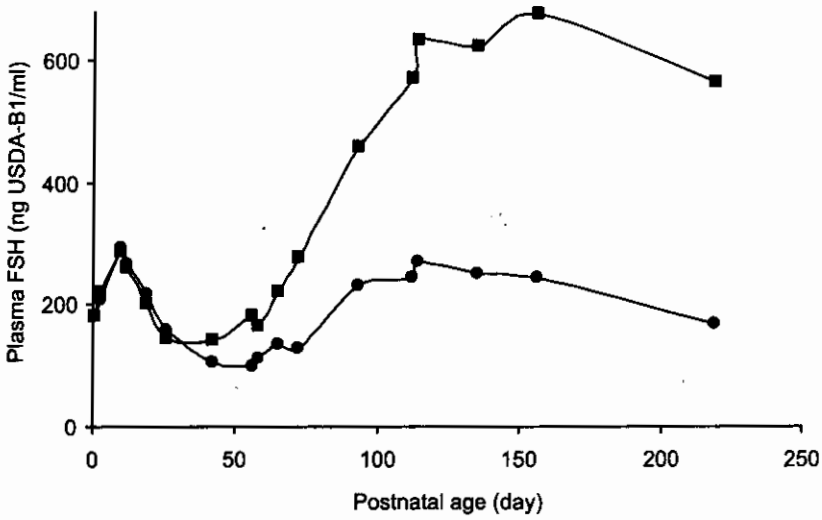

Fig. 5 Plasma concentrations of follicle-stimulating hormone from birth to seven months of age in Meishan (MS (n = 19)) x White composite (WC (n = 18)) boars, adapted from Ford et *al.*, (2001). These boars inherited the testicular size quantitative trait locus of their X chromosome from either the MS or the WC breed.

Thyroid hormones

Thyroid hormones in rodents have direct effects on Sertoli cell proliferation and differentiation. Induction of hypothyroidism during the early postnatal period of Sertoli cell proliferation extends the duration of this proliferative period (i.e., delays terminal differentiation) resulting in greater testicular size and reduced secretion of FSH in adult males (Kirby et *al.*, 1992; Joyce et *al.*, 1993). Conversely, exogenous tri-iodothyronine (T3) in rats induces cessation of mitogenesis and enlargement of the diameter of seminiferous tubules (Francavilla et *al.*, 1991; van Haaster et *al.*, 1993). However, in boars, hypothyroidism during postnatal development fails to increase mature testicular size (Tran et *al.*, 1998; Klobucar et *al.*, 2003). This, combined with the inability of unilateral castration during early postnatal development to produce an increase in number of Sertoli cells in post-pubertal boars that develop small testes, implicated the prenatal period of testicular development as a critical time for establishing the upper limit for number of Sertoli cells (Lunstra et *al.*, 2003).

Crossbred boars with the Meishan QTL for testicular size undergo earlier terminal differentiation of Sertoli cells as evidenced by an earlier enlargement of the diameter of seminiferous tubules. From 75-105 days of gestation, Meishan male foetuses had greater plasma concentrations of T3 and free T3 than WC boars (McCoard et *al.*, 2003a). These findings combined with an operative polymorphism in TBG, a gene within the QTL for testis-size on porcine chromosome X (Rohrer et *al.*, 2001; McCoard et *al.*, 2002a; Nonneman et *al.*, 2005), further link thyroid hormones with the regulation of Sertoli cell proliferation. In addition to its role of transporting T3 and T4 in plasma, TBG can undergo proteolytic cleavage that alters availability of thyroid hormones within tissues (Schussler, 2000).

The hypothesis mentioned above requires that prenatal influences of thyroid hormones impact the timing of Sertoli cell differentiation in postnatal boars, a possibility in agreement with

the inability of unilateral castration during early postnatal development to produce dramatic increases in number of Sertoli cells (Lunstra *et al.*, 2003). However, comparison of thyroid function in Meishan foetuses with that in WC foetuses creates concerns due to differences in body weight and composition of foetuses of these breeds. Thyroid hormones play a critical role in regulating growth, development, differentiation and metabolism of virtually all tissues; thus, inherent metabolic differences between these two diverse breeds should not be ignored as the foundation for the observed differences in plasma T3 concentrations.

Due to the positive correlation of duration of Sertoli cell proliferation with mature testicular size in boars (Lunstra *et al.*, 2003; McCoard *et al.*, 2003b), greater understanding of factors associated with terminal differentiation of porcine Sertoli cells merits further examination to explain genetic differences in sperm production. In rodents, endocrine factors that induce differentiation of Sertoli cells include increased concentrations of testosterone and T3 (Buzzard *et al.*, 2003; Holsberger *et al.*, 2003; Johnston *et al.*, 2004). Again, this rodent model does not relate well to endocrine changes observed in boars where there is not a consistent association of plasma testosterone and T3 with Sertoli cell accumulation. During the first month of life, testosterone secretion in boars is elevated while Sertoli cells are accumulating rapidly (Franca *et al.*, 2000; Ford *et al.*, 2001; McCoard *et al.*, 2003a). After that, accumulation of Sertoli cells ceases before the pubertal increase of testosterone in boars destined to develop small testes (Meishan QTL for testicular size), but this cessation occurs during the pubertal increase of testosterone in boars that develop large testes (WC QTL for testicular size; Ford *et al.*, 2001). Likewise, evidence for a role of T3 in porcine Sertoli cell differentiation is not overwhelming. Secretion of T3 increases abruptly at birth (Slebodzinski and Brzezinska-Slebodzinska, 1994; McCoard *et al.*, 2003a). Moreover, secretion of thyroid-stimulating hormone increases during prepubertal development of boars (Trudeau *et al.*, 1991), but no associated changes in plasma T3 or T4 concentrations are noted at ages corresponding to termination of Sertoli cell proliferation (Tran *et al.*, 1998; Klobucar *et al.*, 2003). Thus, the rodent model for regulatory roles of testosterone and thyroid hormones in Sertoli cell differentiation does not align well with information available in boars.

Thyroid hormones impact cellular function through a family of thyroid hormone receptors (ThR) encoded by 2 genes, *ThRa* and *ThRb*. Both genes can be alternatively spliced giving rise to multiple forms of receptor of which ThRa1, ThRb1 and ThRb2 have been investigated in some detail. ThRa1 is present in Sertoli cells of rodents during neonatal development to provide a means for T3 to impact Sertoli cell proliferation and differentiation (Jannini *et al.*, 1994; Arambepola *et al.*, 1998). Neither the mRNA nor the protein for ThRa1 has been evaluated in porcine testes. The role of ThRb1 in testicular development of rats is controversial; its presence was detected in some studies but not in others (Jannini *et al.*, 1994; Palmero *et al.*, 1995; Buzzard *et al.*, 2000; Canale *et al.*, 2001). Expression of mRNA for ThRb1 occurs in porcine testes (Palmero *et al.*, 1995), but expression profiles and their relationship to development of seminiferous tubules require greater definition. Immuno-detection of ThRb1 reveals a similar profile and relative concentrations in Sertoli cells during foetal development of Meishan and WC boars, and relative prenatal concentrations reach a maximum at the time the highest percentage of Sertoli cells are undergoing proliferation (McCoard *et al.*, 2003a). Thus, the pattern of expression of ThRb1, accommodates a role for establishing testicular size in boars if it is the primary mediator of T3 effects on porcine Sertoli cells. Collectively, the current state of knowledge of endocrine changes in boars is inadequate to lead to a convincing hypothesis to explain breed differences in testicular size and sperm production.

Conclusions

Developmental patterns of change in the seminiferous tubules of Meishan and WC foetal boars are astonishingly similar in spite of the much earlier age of pubertal development and smaller mature testicular size of Meishan compared with WC boars. Introduction of this diverse breed of pigs from China provided a valuable animal model for investigation of testicular development. Clearly, early cessation of Sertoli cell proliferation accounts for small testicular size in this breed; however, boars of the Piau breed have small testicles, but they achieve this through a longer period of Sertoli cell proliferation and a greater proportion of their testes occupied with seminiferous tubules. Mass of seminiferous tubules in boars is unmistakably a heritable trait and is the primary determinant for daily sperm production. A region on the q arm of the X chromosome contributes to variation in the quantity of seminiferous tubules in Meishan crossbred boars, but studies are required to establish the genetic basis for differences in daily sperm production of other breeds of boars.

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