The association of two single nucleotide polymorphisms (SNPs) in growth hormone (GH) gene with litter size and superovulation response in goat-breeds

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Abstract
Two active mutations (A 781 G and A 1575 G) in growth hormone (GH) gene, and their associations with litter size (LS), were investigated in both a high prolificacy (Matou, n = 182) and a low prolificacy breed (Boer, n = 352) by using the PCR-RFLP method. Superovulation experiments were designed in 57 dams, in order to evaluate the effect of different genotypes of the GH gene on superovulation response. Two genotypes (AA and AB, CC and CD) in each mutation were detected in these two goat breeds. Neither BB nor DD homozygous genotypes were observed. The genotypic frequencies of AB and CC were significantly higher than those of AA and CD. In the third parity, Matou dams with AB or CC genotypes had significantly larger litter sizes than those with AA and CD (p < 0.05). On combining the two loci, both Matou and Boer dams with ABCD genotype had the largest litter sizes when compared to the other genotypes (p < 0.05). When undergoing like superovulation treatments, a significantly higher number of corpora lutea and ova, with a lower incidence of ovarian cysts, were harvested in the AB and CC genotypes than in AA and CD. These results show that the two loci of GH gene are highly associated with abundant prolificacy and superovulation response in goat breeds.

Key words: DNA polymorphism, growth hormone (GH) gene, litter size, superovulation response, goat.

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Introduction
It has been reported that metabolic hormones, such as growth hormone (GH), are directly involved in mediating nutritionally-induced changes in follicular development (Downing and Scaramuzzi, 1991; Prunier and Quesnel, 2000; Armstrong et al., 2003). The growth hormone of mammals plays an important role in the control of reproduction, in those aspects involving cell division, ovarian folliculogenesis, oogenesis and secretory activity (Schams et al., 1999; Gong, 2002; Hull and Harvey, 2002; Ola et al., 2008). By acting through specific receptors within the ovary, GH is expedient in controlling proliferation and apoptosis, oocyte maturation, and the expression and synthesis of receptors to hormones and related substances (Sirotkin et al., 1998; Schams et al., 1999; Hull and Harvey, 2000; Sirotkin et al., 2003). The addition of bovine GH during in vitro maturation (IVM) of bovine oocytes has been found to induce cumulus expansion and accelerate nuclear maturation, besides promoting subsequent fertilization, cleavage and early embryonic development, as shown by enhancing the number of resultant blastocysts (Izadyar et al., 1996, 1998; Joudrey et al., 2003). Further studies have revealed that the effect of GH on ovary function is mainly through inducing the development of small antral follicles in the gonadotrophin-dependent stages and stimulating oocyte maturation (Silva et al., 2009).

As abundantly illustrated in the literature, numerous attempts have been made to investigate the effects of the GH gene on mammal growth and milk production (Wang et al., 2003; Gupta et al., 2007; Hua et al., 2008; Balogh et al., 2009; McCormack et al., 2009), with only few reported studies of this in oogenesis and spermiogenesis (Kmie et al., 2007; Murphy et al., 2008), and no mention of the effects on litter size and superovulation response. To date, little has been divulged on the major gene associated with litter size in goats, these few studies involving the inhibin alpha-subunit gene (INHA) (Hua et al., 2008; Wu et al., 2009), the gonadotrophin releasing hormone receptor gene (GnRHR) (An et al., 2009), the bone morphogenetic protein receptor-IB gene (BMPRIB) in the prolific Indian Black Bengal goat (Polley et al., 2009), and the bone morphogenetic protein 15 gene (BMP15) in Jining Grey goats (Chu et al., 2007).
Growth and reproduction, two crucial economic traits in production, are co-ordinated during normal puberty and the adult stages. There is evidence that normal growth-hormone secretion is required for the correct timing of the onset of puberty (Franks et al., 1998). As already confirmed in our previous research, there is a significantly positive association of two polymorphisms (A 781 G and A 1575 G) of GH gene with growth in Boer bucks (Hua et al., 2008). Consistent with the essential function of GH in puberty and ovary activity, there is the need for further validation regarding its effects on dam reproduction.

Hence, in this study, the relatively hyper-prolific Matou breed and the low-prolific Boer were used to investigate the frequency distribution of the two GH gene polymorphisms (A 781 G and A 1575 G), and evaluate their effects on litter size. We contemplated factors affecting litter size, including year, season and parity, besides the age of the dam, with due account also being given to their mutual interactions. Furthermore, specific experiments were designed to evaluate the superovulation response in dams with different GH genotypes.

Materials and Methods

Data collection from experimental goat breeds

All procedures involving animals were approved and authorized by the Chinese Ministry of Agriculture, through the Animal Care and Use Committee at the respective institution where the experiment was undertaken.

A total of 534 adult females from two goat breeds differing in prolificacy, viz., 352 Boer dams with records of 1188 parities and 182 Matou dams with records of 583 parities, were analyzed in the present study. Those from the Boer breed, the low-prolific line (LS = 1.42) obtained from the Yidu Boer-Goat Breeding Station, had four depth levels of generation in the pedigree consisting of 129 sires and 552 dams, whereas the Matou breed, the native hyper-prolific line (LS = 2.14), collected from farms in Shiyan county, presented three generation depth levels in the pedigree.

Blood collection and genomic DNA preparations were carried out according to Hua et al. (2008). The data regarding litter size (LS) were collected in consecutive parities, considering repeated measurements in the same individual. Due to the significant effect of parity on litter size in goats, and its stability following the third parity (Moeenud-Din et al., 2008; Wu et al., 2009; Zhang et al., 2009), the data were calculated separately for primiparity, third parity and all the parities together.

Superovulation dams and sampling

A total of 57 adult native, fertile females in healthy conditions were used in superovulation experiments. The dams, selected under similar and uniform conditions, taking into account age (3 to 5 years) and body weight (35 to 40 kg), were raised for about 2 weeks prior to the outset of superovulation. All the animals were barn housed and under controlled nutrition. The diet was a mixture of cured hay and grains, with a daily vitamin supplement. Fresh water and a mineral supplement were available ad libitum.

Superovulation procedure and response

The synchronization of estrus was induced by the administration of a single minuscule injection of Clopoprostanol Sodium (PG-Cl), in a dose of 0.2 mg, on the day prior to initiating the experiment. Beginning on the 2nd day, Pituitary Follitropin for Capra (cFSH) was given twice daily at intervals of 12 h in eight decreasing doses (40, 40, 30, 30, 20, 20, 20, and 20 IU). The last cFSH dose was given concurrently with a single 25 μg dose of Luteinizing Hormone Releasing Hormone A3 (LHRH-A3). All the experimental dams were slaughtered on the 7th day, whereupon the ovaries and oviducts were collected and kept in incubation casks (37 °C) containing PBS, and brought to the laboratory within 1 h. The whole experiment, which took place in November, was undertaken with hormones provided by the Ningbo Sansheng Pharmaceutical Co., Ltd., Ningbo, China, all from single batches.

The ova were recovered by aspiration from the oviducts, and searched immediately after filtering the aspirated follicular fluid medium. The numbers of follicles of different sizes on ovarian surfaces were evaluated, based on a classification of follicle diameters as small (< 2.0 mm), medium (2.0 ~ 4.0 mm), large (4.0 ~ 8.0 mm) and ovarian cyst (> 8.0 mm) (Valasi et al., 2007). The total number of ova, corpora lutea and ovarian cysts, per dam and in each class, were recorded. All the observations were done by one and the same person using the same methodology throughout.

Primer synthesis and polymerase chain reaction-restriction fragment length polymorphism (PCR-RFLP) analysis

Our previous report (Hua et al., 2008) formed the base for designing primer and setting PCR conditions. Two amplicons of 422 bp and 116 bp were yielded by the PCR reaction using the following primers synthesized by Shanghai Sangon Biotech Co., Ltd.:

GH1: 5'-CTCTGCCTGCCCCTGGACT-3’ and 5'-GGAAGAGCAGAGGCAAC-3’
GH2: 5'-TCAGCAGAGTCTTCCAACC-3’ and 5'-CACAACGCCATCCTCAC-3’

The Forced PCR-RFLP method was used to detect the A 781 G and A 1575 G mutations. The PCR products were digested by HaeIII restriction endonuclease (TaKaRa, Tokyo, Japan) at 37 °C for 12-14 h with the following reaction system: a final volume of 10 μL containing 4 μL of the PCR product, 4 U of the HaeIII enzyme and 1 x buffer R. In order to improve resolving power and accuracy, 8% polyacrylamide gel electrophoresis (PAGE), and, subsequently,
silver staining, were used for detecting the reaction products. *PBR322/MspI* (HuaMei Bioengineering Co., Ltd., China) was employed as a size marker for defining restriction-fragment sizes.

**Statistical analysis**

The allelic and genotypic frequencies in the *GH* gene in both goat breeds were analyzed. A Bonferroni correction (derivative-free restricted maximum likelihood, DFREML) was used to analyze the relationship between *GH* gene and litter size with animal models (Meyer and Kirkpatrick, 2005). Pedigrees of base population animals were traced back three (Matou) or four (Boer) generations, in order to create the numerator relationship matrix.

All the analyses were carried out in two steps, first using a full animal model and then using a reduced animal model. The full-animal model included all the factors, viz., genotypes, parity (1, 2, 3, 4 and ≥ 5), age of dam (1, 2, 3 and ≥ 4 years), kidding year (2002-2009), four kidding seasons – Spring (March and April), Summer (May to September), Autumn (October and November), and Winter (December to February), as well as the interactions of year-season, year-parity, parity-season and parity-age. Data of litter size from consecutive parities in the same individual were considered as repeated measures, and included in the statistical model. The reduced-model included only those fixed effects (genotype, kidding year, parity and age of the dam) that exerted a significant influence on LS (p < 0.05), and was only used in the final analysis. The reduced-animal model was:

\[ y = Xb + Za + Zp + e \]

where \( y \) is a vector of observations for litter size, \( b \) a vector of fixed effects for genotype, kidding year, parity and age of the dam, \( a \) a vector of animal genetic effects, \( p \) a vector of permanent environmental effects for parities of each dam, and \( e \) a vector of random residual effects. When analyzing the phenotypic data of primiparity and the third parity, the parity effect was excluded.

Data on superovulation response were analyzed statistically by applying the one-way ANOVA of SAS procedures (SAS Institute, Cary, NC, USA). The significance of the difference was determined by F-test at the significance level of 0.05.

**Results**

**PCR amplification and RFLP analysis**

As expected, two fragments of the *GH* gene (422 and 116 bp) were amplified from caprine genomic DNA by the *GH1* and *GH2* primers. Both fragments, when digested by endonuclease *Hae*III, resulted in four genotypes named: AA (366 and 56 bp) and AB (422, 366 and 56 bp) for *GH1*, and CC (88 and 28 bp) and CD (116, 88 and 28 bp) for *GH2* (Figure 1). Thus, in the 534 individuals from the 2 differently prolific breeds, four genotypes of the two fragments of the *GH* gene were detected in both the Matou and Boer breeds, but no homozygotes of either BB or DD individuals were found (Figure 1).

**Allele genotypic and haplotypic frequencies of GH gene in the two goat breeds**

The genotypic and haplotypic frequencies of sequence polymorphisms are given in Table 1. The frequencies of AB and CC genotypes were much higher than those of AA and CD in both goat breeds. On comparing the same genotypic frequency between the two breeds, that of AB and CC genotypes in the Matou breed was much higher than in the Boer. When combining the two loci, the frequency of the ABCC haplotype proved to be the highest and that of the AACD the lowest.

**Influence of genotype on litter size**

The association of independent genotypes in *GH* gene with litter size, in Boer and Matou dams, is given in Table 2. In various parity groups, Matou dams with AB or CC genotypes had larger litter sizes than those with AA or CD (p < 0.05), although no significant difference appeared at

**Figure 1** - Polyacrylamide gel electrophoresis (PAGE) profile for *Hae*III digestion products of *GH1* (AA and AB) and *GH2* (CC and CD). Lanes 2 to 4 represent digestion products from samples with the CD genotype (116, 88 and 28 bp). Lanes 5 to 7 represent the CC genotype (88 and 28 bp). Lanes 8 and 9 represent the AA genotype (366 and 56 bp). Lanes 10 to 13 represent the AB genotype (422, 366 and 56 bp). Small fragments of 28 bp and 56 bp were invisible in the gel. Lanes 1 and 14 show the PBR322/MspI DNA marker.
Table 1 - Sample size, and genotypic and haplotypic frequencies of GH polymorphisms in Boer and Matou goat breeds.

| Breeds | N   | A 781 G | A 1575 G | Haplotype |
|--------|-----|---------|----------|-----------|
|        |     | AA      | AB       | CC        | CD        | ABCC | ABCD | AACC | AACD |
| Boer   | 352 | 0.233 (82) | 0.767 (270) | 0.776 (273) | 0.224 (79) | 0.648 (228) | 0.119 (42) | 0.128 (45) | 0.105 (37) |
| Matou  | 182 | 0.165 (30) | 0.835 (152) | 0.846 (154) | 0.154 (28) | 0.735 (134) | 0.100 (18) | 0.110 (20) | 0.055 (10) |
| Total  | 534 | 0.210 (112) | 0.790 (422) | 0.799 (427) | 0.201 (107) | 0.678 (362) | 0.112 (60) | 0.122 (65) | 0.088 (47) |

Numbers in parentheses indicate sample size.

Table 2 - Effects of separate GH gene genotypes on litter size in primiparity, the third parity and all the parities in Boer and Matou dams (means ± SD).

| Parity groups | Breeds | A 781 G | A 1575 G | p-value |
|---------------|--------|---------|----------|---------|
| Primiparity   | Boer (352) | 1.42 ± 0.51 (82) | 1.54 ± 0.71 (270) | 0.6160 |
|               | Matou (182) | 1.69 ± 0.60 (30) | 1.88 ± 0.77 (152) | 0.6029 |
| Third parity  | Boer (290) | 1.81 ± 0.81 (62) | 1.87 ± 0.63 (228) | 0.8196 |
|               | Matou (156) | 2.04 ± 0.76 (25) | 2.62 ± 0.89 (131) | 0.0158 |
| All parities  | Boer (352) | 1.80 ± 0.73 (82) | 1.81 ± 0.65 (270) | 0.9341 |
|               | Matou (182) | 1.93 ± 0.65 (30) | 2.37 ± 0.91 (152) | 0.0036 |

Numbers in parentheses indicate sample size.

Table 3 - Effects of combined GH gene genotypes on litter size in primiparity, the third parity and all the parities in Boer and Matou dams (means ± SD).

| Parity groups | Breeds | A 781 G | A 1575 G | p-value |
|---------------|--------|---------|----------|---------|
| Primiparity   | Boer (352) | 1.33 ± 0.57 (37) | 1.44 ± 0.53 (45) | 1.53 ± 0.70 (228) | 1.61 ± 0.78 (42) |
|               | Matou (182) | 1.50 ± 0.55 (10) | 1.62 ± 0.57ab (20) | 1.80 ± 0.79ab (134) | 2.00 ± 0.71b (18) |
| Third parity  | Boer (290) | 1.50 ± 1.00ab (23) | 1.88 ± 0.78ab (39) | 1.84 ± 0.62ab (196) | 2.04 ± 0.65b (32) |
|               | Matou (156) | 2.00 ± 0.81a (8) | 2.17 ± 0.00ab (17) | 2.25 ± 0.87ab (116) | 2.55 ± 1.03 (15) |
| All parities  | Boer (352) | 1.45 ± 0.71 (37) | 1.76 ± 0.73 (45) | 1.80 ± 0.64 (228) | 1.88 ± 0.74 (42) |
|               | Matou (182) | 1.73 ± 0.47 (10) | 1.97 ± 0.68ab (20) | 2.02 ± 0.90ab (134) | 2.37 ± 0.90b (18) |

Numbers in parentheses indicate sample size.

Values marked in different superscripts on the same row (small letters) were significantly different (p < 0.05).
Gene variants of the GH gene associated with reproduction in goats have been detected, most of which involving growth traits. To date, more than 10 goat GH gene variants have been studied. To date, more than 10 goat GH gene variants have been studied. To date, more than 10 goat GH gene variants have been studied.

Influence of the genotype on litter size and superovulation response

The association analysis showed that the different genotypes or haplotypes have significant effects on litter size and superovulation response. This is the first time that the effects of GH gene polymorphism on goat reproduction have been studied. To date, more than 10 goat GH variants have been detected, most of which involving growth traits (Gupta et al., 2007; Hua et al., 2008), and a few milk production (Malveiro et al., 2001; Marques et al., 2003). Nevertheless, no report has focused on reproduction traits. Our previous research has already confirmed that these two mutations of the GH gene exerted a highly additive effect on growth traits in Boer bucks (Hua et al., 2008). The crucial role of GH in oogenesis and follicular development has been amply confirmed (Schams et al., 1999; Sirotkin et al., 2003; Silva et al., 2009). Hence, the present study was designed to be a continuing step in evaluating the effect of the GH gene on litter-size and superovulation, with a mind to eventually providing further useful and detailed information for molecular marker-associated selection (MAS) programs.

Table 4 - Effects of GH gene genotypes on the numbers of corpora lutea (NCL), follicles of different size and ova harvested, as well as the incidence of ovarian cysts after superovulation (means ± SD).

| Genotype | Follicle size in diameter (mm) | NCL | Ova harvested | Incidence of ovarian cysts (%) |
|----------|-------------------------------|-----|---------------|-------------------------------|
|          | Small (< 2.0) | Medium (2.0~4.0) | Large (4.0~8.0) |       |          |          |
| AA (20)  | 8.3 ± 2.9 | 5.1 ± 1.8 | 5.7 ± 3.4 | 6.6 ± 2.6 | 4.4 ± 2.1 | 50.0 (10/20) |
| AB (37)  | 12.4 ± 2.3 | 8.4 ± 2.9 | 6.5 ± 2.5 | 11.7 ± 3.1 | 10.6 ± 3.3 | 27.0 (10/37) |
| p-value  | 0.2069 | 0.1105 | 0.4798 | 0.0379 | 0.0488 | - |
| CC(49)   | 12.1 ± 3.8 | 9.3 ± 2.1 | 6.4 ± 2.6 | 11.7 ± 3.9 | 9.8 ± 3.4 | 22.4 (11/49) |
| CD(8)    | 9.0 ± 2.5 | 5.8 ± 2.3 | 5.9 ± 3.5 | 5.0 ± 2.1 | 5.5 ± 2.0 | 37.5 (3/8) |
| p-value  | 0.5611 | 0.4508 | 0.4191 | 0.0349 | 0.0782 | - |

Numbers in parentheses indicate sample size. p-values for F-test.

gous were observed in any individual whatsoever. Our previous research on the GH gene also revealed this to be the case in 154 Boer bucks (Hua et al., 2008), as was also reported in Chengdu-Ma (n = 37) and Boer (n = 29) goats (Bai et al., 2005), and in a Gannan Yak population (n = 202) (Bai et al., 2009). The A 781 G polymorphism was also detected in other goat flocks, such as the LuBei white goat (n = 50), and in the first filial generation of LuBei white and Boer (n = 105) goats (Li et al., 2004).

All told, BB and DD genotypes were absent in both females and males in seven goat breeds, this including purebreds and crossbreds, as well as in Yaks, as mentioned above. It has been amply confirmed in the literature that the GH gene is essential for normal reproductive functions including oogenesis, follicular development and embryogenesis (Sirotkin et al., 1998, 2003; Schams et al., 1999; Hull and Harvey, 2000; Ola et al., 2008; Silva et al., 2009). Thus, it can be presumed that A 781 G (BB) and A 1575 G (DD) homozygous mutations in the GH gene may give rise to reproductive disturbance, even to the point of infertility.

The separation of AB and CC genotypes has been associated with larger litter sizes and a higher superovulation response. This effect is most likely due to allelic interaction and the important biological effects of GH on reproduction processes, this including oogenesis, follicular development and embryogenesis. It has been reported that, on initiating cattle superstimulation protocols, pre-treatment with growth hormone can increase the population of antral follicles (Bols et al., 1998; Gong, 2002). Knockout experiments have demonstrated that GH enhances the development of small antral follicles up to the gonadotrophin-dependent stage, besides stimulating oocyte maturation (Silva et al., 2009). The addition of bGH during in vitro maturation (IVM) of bovine oocytes has been found to induce cumulus expansion, besides accelerating nuclear maturation reflected by the accelerated extrusion of the 1st polar body, and promoting subsequent fertilization, cleavage and early embryonic development (Izadyar et al., 1996, 1998). Kölle et al. (2001) reported that the GH gene is also involved in activating cellular functions in blastocysts, thereby stimulating glucose uptake and protein synthesis. Joudrey et al. (2003) reported that during bovine embryogenesis, bovine growth hormone contributes to proliferation, differentiation, and modulation of embryonic metabolism. The absence of BB and DD genotypes, as observed in the present and previous research, further confirmed the significance of GH in goat reproduction and growth.

When combined, the two SNPs displayed more profound impacts on LS than separately in both goat breeds. Both Boer and Matou dams with the ABCD genotype had the largest litter sizes compared to the others, and the combined genotype AADC was associated with the lowest litter sizes. This is consistent with previous research on goat growth traits by Hua et al. (2008), who reported that body weight and growth rate from birth to weaning was the lowest in Boer bucks bearing the AADC genotype,
whereby it can be concluded that goats with this genotype should be avoided in selection programs.

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References

An XP, Han D, Hou JX, Li G, Wang JG, Yang MM, Song YX, Zhou GQ, Wang YN and Ling L (2009) GnRHR gene polymorphisms and their effects on reproductive performance in Chinese goats. Small Rumin Res 85:130-134.

Armstrong DG, Gong JG and Webb R (2003) Interactions between nutrition and ovarian activity in cattle: Physiological, cellular and molecular mechanisms. Reproduction 61:403-414.

Bai WL, Wang J and Yin RY (2005) Study on genetic polymorphism of HaeIII site of GH gene in Chengdu-Ma goat and Boer goat. Heilongjiang Anim Sci and Vet Med 8:13-14.

Bai JJ, Wang JQ, Hu J and Luo YZ (2009) SNPs detection of growth hormone gene in Gannan Yak population. China Cattle Sci 25:1-5.

Balogh O, Kovács K, Kulcsár M, Gáspárda Y, Zsolnai A, Kátai L, Pécsi A, Fész L, Butler WR and Huszenicza GY (2009) AluI polymorphism of the bovine growth hormone (GH) gene, resumption of ovarian cyclicity, milk production and loss of body condition at the onset of lactation in dairy cows. Theriogenology 71:553-559.

Bols PE, Ysebaert MT, Lein A, Coryn M, Van Soom A and de Kruif A (1998) Effects of long-term treatment with bovine somatotropin on follicular dynamics and subsequent oocyte and blastocyst yield in an OPU-IVF program. Theriogenology 49:983-995.

Chu MX, Jiao CL, He YQ, Wang JY, Liu ZH and Chen GH (2007) Association between PCR-SSCP of bone morphogenetic protein 15 gene and prolificacy in Jining Grey goats. Anim Biotechnol 18:263-274.

Downing JA and Scaramuzzi RJ (1991) Nutrient effects on ovulation rate, ovarian function and the secretion of gonadotrophic and metabolic hormones. J Reprod Fertil Suppl 43:209-227.

Franks S, Frec MD and Horz MD (1998) Growth hormone and ovarian function. Baillieres Clin Endocrinol Metab 12:331-340.

Gong JG (2002) Influence of metabolic hormones and nutrition on ovarian follicle development in cattle: Practical implications. Domest Anim Endocrinol 23:229-241.

Gupta N, Ahlawat SPS, Kumar D, Gupta SC, Pandey A and Malik G (2007) Single nucleotide polymorphism in growth hormone gene exon-4 and exon-5 using PCR-SSCP in Black Bengal goats - A prolific meat breed of India. Meat Sci 76:658-665.

Hua GH, Chen SL, Yu JN, Cai KL, Wu CJ, Li QL, Zhang CY, Liang AX, Han L and Geng LY (2008) Polymorphism of the growth hormone gene and its association with growth traits in Boer goat bucks. Meat Sci 81:391-395.

Hull KL and Harvey S (2002) GH as a co-gonadotropin: The relevance of correlative changes in GH secretion and reproductive state. J Endocrinol 172:1-19.

Izadyar F, Colenbrander B and Bevers MM (1996) In vitro maturation of bovine oocytes in the presence of growth hormone accelerates nuclear maturation and promotes subsequent embryonic development. Mol Reprod Dev 45:372-377.

Izadyar F, Hage WJ, Colenbrander B and Bevers MM (1998) The promotory effect of growth hormone on the developmental competence of in vitro matured bovine oocytes is due to improved cytoplasmic maturation. Mol Reprod Dev 49:444-453.

Joudrey EM, Lechniak D, Petrlik J and King WA (2003) Expression of growth hormone and its transcription factor, Pit-1, in early bovine development. Mol Reprod Dev 64:275-283.

Knie M, Terman A, Wierzbicki H and Zych S (2007) Association of GH gene polymorphism with semen parameters of boars. Acta Vet Brno 76:41-46.

Kölle S, Stojkovic M, Prellke L, Watera M, Wolf E and Sinowatz F (2001) Growth hormone (GH)/GH receptor expression and GH-mediated effects during early bovine embryogenesis. Biol Reprod 64:1826-1834.

Li M, Pan Y, Pan QH, Shen YC, Min W and Ren LJ (2004) Polymorphism analysis of goat growth hormone (GH) gene by PCR-RFLP. J Laiyiang Agr Res 21:6-9.

Malveiro E, Pereira M, Marques PX, Santos IC, Belo C, Renaville M and Cravador A (2001) Polymorphisms at the five exons of the growth hormone gene in the algarvia goat: Possible association with milk traits. Small Rumin Res 41:163-170.

Marques PX, Pereira M, Marques MR, Santos IC, Belo CC, Renaville R and Cravador A (2003) Association of milk traits with SSCP polymorphisms at the growth hormone gene in the Serrana goat. Small Rumin Res 50:177-185.

McCormack BL, Chase Jr CC, Olson TA, Elsasser TH, Hammond AC, Welsh Jr TH, Jiang H, Randel RD, Okamura CA and Lucy MC (2009) A miniature condition in Brahman cattle is associated with a single nucleotide mutation within the growth hormone gene. Domest Anim Endocrinol 37:104-111.

Meyer K and Kirkpatrick M (2005) Restricted maximum likelihood estimation of genetic principal components and smoothed covariance matrices. Genet Sel Evol 37:1-30.

Moanen-ud-Din M, Yang LG, Chen SL, Zhang ZR, Xiao JZ, Wen QY and Dai M (2008) Reproductive performance of Matou goat under sub-tropical monsoonal climate of Central China. Trop Anim Health Prod 40:17-23.

Murphy AM, Meade KG, Hayes PA, Park SDE, Evans ACO, Lonergan P and MacHugh DE (2008) Transmission ratio distortion at the growth hormone gene (GH1) in bovine preimplantation embryos: An in vitro culture-induced phenomenon? Mol Reprod Dev 75:715-722.

Ola SI, Ai JS, Liu JH, Wang Q, Wang ZB, Chen DY and Sun QY (2008) Effects of gonadotrophins, growth hormone, and activin A on enzymatically isolated follicle growth, oocyte chromatin organization, and steroid secretion. Mol Reprod Dev 75:89-96.
Polley S, De S, Batabyal S, Kaushik R, Yadav P, Arora JS, Chattopadhyay S, Pan S, Brahma B and Datta TK (2009) Polymorphism of fecundity genes (BMPR1B, BMP15 and GDF9) in the Indian prolific Black Bengal goat. Small Rumin Res 85:122-129.

Prunier A and Quesnel H (2000) Influence of the nutritional status on ovarian development in female pigs. Anim Reprod Sci 61:185-197.

Schams D, Berisha B, Kosmann M, Einspanier R and Amsel-gruber WM (1999) Possible role of growth hormone, IGFs, and IGF binding proteins in the regulation of ovarian function in large farm animals. Domest Anim Endocrinol 17:279-285.

Silva JRV, Figueiredo JR and van den Hurk R (2009) Review: Involvement of growth hormone (GH) and insulin-like growth factor (IGF) system in ovarian folliculogenesis. Theriogenology 71:1193-1208.

Sirotkin AV, Makarevich AV, Kotwica J, Marnet PG, Kwon HB and Hetenyi L (1998) Isolated porcine ovarian follicles as a model for the study of hormone and growth factor action on ovarian secretory activity. J Endocrinol 159:313-323.

Sirotkin AV, Mertin D, Süvegová K, Makarevich AV and Mikulová E (2003) Effect of GH and IGF-I treatment on reproduction, growth, and plasma hormone concentrations in domestic nutria (Myocastor coypus). Gen Comp Endocrinol 131:296-301.

Valasi I, Leontides L, Menegatos I and Amiridis GS (2007) Oestradiol concentration as a predictor of ovarian response in FSH stimulated ewe-lambs. Anim Reprod Sci 102:145-151.

Wang WJ, Huang LS, Gao J, Ding NS, Chen KF, Ren J and Luo M (2003) Polymorphism of growth hormone gene in 12 pig breeds and its relationship with pig growth and carcass traits. Asian Austral J Anim 16:161-164.

Wu WS, Hua GH, Yang LG, Wen QY, Zhang CY, Khairy MZ and Chen SL (2009) Association analysis of the INHA gene with litter size in Boer goats. Small Rumin Res 82:139-143.

Zhang CY, Chen SL, Li X, Xu DQ, Zhang Y and Yang LG (2009) Genetic and phenotypic parameter estimates for reproduction traits in the Boer dam. Livest Sci 125:60-65.

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