

Phenotypic and genetic characteristics of fecundity in sheep. A review

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Abstract

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The phenotypic characteristics of animals are result of the complex interaction of a number of genetic and non-genetic factors, which usually act simultaneously and it is difficult to determine the degree of influence of each of them. Early identification of the genetic traits of individuals enables more efficient management of selection. Fertility determines the cost-effectiveness of sheep farming, regardless of productive direction. The individual fertility of the animals is determined by the number of lambs born per sheep. This trait is characterized by a low inheritance rate, hence conventional breeding methods shows slow progress. The introduction of new molecular-based technologies to improve productivity contributes to a greater and faster effect on the realization of animal genetic resources. The assessment of the breeding value of animals at the earliest possible age makes it possible to maximize the effect of the selection and to increase the use of animals with the highest genetic potential. The molecular markers and the application of RFLP-PCR method allow the determination of allelic variants of genes related to the quantity and quality of animal productivity. By identifying the different polymorphic variations and their phenotypic manifestation, a database can be accumulated to manage the genetic progression of economically important traits. Many mutations have been found in sheep that affect fertility and ovulation rates to varying degrees. Large number of mutations which affects ovulation have been found in genes expressing different proteins, such as the *BMPRI1B* or *FecB* (Booroola gene or the bone morphogenetic protein receptor type 1B), *GDF9* or *FecG* (the growth differentiation factor 9b) and *BMP15* or *FecX* (a bone morphogenetic protein 15).

Keywords: fecundity in sheep; marker assisted selection; molecular marker applications; gene expression

Introduction

Classical selection methods are based on the evaluation of the additive genetic component of traits, using different models depending on variation, heritability, generation interval, accuracy of breeding value assessment and intensity of selection. Significant genetic progress is being made with this breeding technique, but the introduction of new molecular-based technologies to improve productivity will contribute to a greater and faster effect on the realization of animal

genetic resources. Assessment of breeding value of animals at the earliest possible age makes it possible to maximize the effect of the breeding and timely intensive use of the animals with the highest genetic resources. Molecular markers and the use of RFLP-PCR method allow the determination of allelic variants of genes related to the quantity and quality of animal productivity. By identifying the different polymorphic variations and their phenotypic manifestation, a database can be accumulated to manage the genetic progression of economically important traits.

Phenotypic characteristics

The factors affecting the phenotypic characteristics in sheep are hereditary and non-hereditary (extrinsic), usually acting simultaneously, making it difficult to determine the extent of the influence of each of them. The establishment of the genetic potential of the animals makes the control of the selection more efficient.

The fertility is an important trait determining the productivity in sheep breeding but also is a main factor associated with the economic efficiency regardless of the productive direction.

Fertility is a significant characteristic of economical importance in sheepbreeding in Bulgaria, Hinkovski (1972) in Askanian sheep and Dimitrov (1978) in Ile de France found increase of the mothers' fertility with age as this continues up to 6 years. The phenotypic characteristics in sheep are a result of the complex interaction of a wide range of genetic and non-genetic factors. According to the existing studies about dairy sheep, the fertility ranges considerably.

Djorbineva (1984) when studying the selection traits of local Stara Zagora sheep observed low to medium fertility in the range of 1.214 to 1.412, with variation coefficients within the range of 31.44% to 52.95%. For purebred local Stara Zagora sheep from different flocks Djorbineva et al. (2011) reported variation in the values of prolificacy within 123.4% to 157.4%. Similar results about this trait within the normal range in local dairy sheep have been reported by Dimov (2000) in splotch-faced Maritsa sheep at first and second lactation- 1.193 and 1.454, respectively.

Stancheva (2003) found prolificacy of sheep from Bulgarian dairy synthetic population in the process of its formation as follows: 1.335 (at first lactation) and 1.412 (at second lactation). These values are close to the ones that have been reached by the breed at its contemporary state. The year of birth has significant effect on the prolificacy of the same flock in Shumen, as the authors report about 1.33 lambs born by a single sheep at first lactation and 1.41 – at the second lactation (Boikovski et al., 2003).

Hinkovski et al. (2008) at the analysis of the results about the biological fertility of the studied flock reported mean value of the trait 1.31 (1.3 – at the first and 1.24 – at the second lactation), and did not find significant differences among the animals at different lactations. Concerning the same flock Metodiev et al. (2010) while testing the effect of the salt-free/salt diet and the effect of the ram on the reproductive traits of the sheep, recorded average fertility of 127.27%, as for the sheep at first lactation it is 125.9%, and at the second – 136.8%.

In a publication by Ivanova et al. (2010), treating the relations between the exterior measurements and the performance traits in Bulgarian dairy synthetic population ewes at first lactation, prolificacy was reported to be 1.5 lambs per ewe.

Thomas et al. (1999) found high (1.93 lambs) fertility in East Friesian crosses at different age. In another study with crossbreeds (East Friesian and Lacaune), the authors reported fertility of 1.52 lambs (Thomas et al., 2000). At later stage in a study with the same kind of crossbreeds, they did not find significant differences in the fertility of the sheep at first (1.56 lambs) and second (1.65 lambs) lactation (Thomas et al., 2010).

High fertility (1.72 lambs) was reported by Kominakis et al. (2009) in the Greek dairy breed Frizarta, formed with the participation of the East Friesian sheep.

In meat sheep Suffolk-Hampshire in the reproductive non-reproductive period Martínez et al. (2017) reported the following results: in the reproductive period 90% of ewes presented estrus and in the non-reproductive period 100%, the percentage of fertility was 80 and 100% respectively and prolificacy was 1.3 and 1.0 lambs born per ewe respectively.

Hackett and Wolynetz (1985) studied the reproductive performance (fertility and prolificacy) of Finnish Landrace (Finn) and Suffolk sheep. The results pointed to a higher fertility for Finn ewes than for Suffolk ewes. Higher prolificacy was observed in the Finn ewes than in the Suffolk ewes, but the differences in prolificacy varied with the month of breeding. The probability of a ewe having more than one lamb was significantly higher for Finn ewes than for Suffolk ewes in both January and May breedings, but was similar in September breedings.

Fadare (2015) evaluated the reproductive performance of sheep with black, white and brown wool, measuring prolificacy and fecundity. Prolificacy of the different colour types ranged between 1.58 and 1.18; black colour ewes had the highest prolificacy. The black ewe also had the greatest fecundity (2.50). Parity of the ewes as well as season of lambing also had significant effect on the traits measured. Black ewes were superior to other colour types with regards to the reproductive traits.

Kridli et al. (2009) studied the effect of breed types and lactation status on reproductive performance of Awassi ewes. The percentage of multiple births, fecundity and prolificacy were greater in black-faced ewes (48.1%, 1.27 and 1.56) according to brown-faced ewes (26.2%, 0.99 and 1.32). The percentage of multiple births was 32.4% for lactating ewes and 24.2% for dry ewes. Fecundity tended to be greater in lactating ewes (1.24) ($P < 0.1$), while prolificacy was similar regardless of lactation status (1.39 and 1.30).

Hansen and Shrestha (1997) observed three synthetic sheep breeds (Canadian, Outaouais and Rideau Arcotts) where ewes were mated to lamb in February, June and October at intervals in an 8 month breeding cycle. Traits examined included fertility, prolificacy, multiple birth, fecundity. The study demonstrates that there is significant potential to genetically increase reproductive rate in Canadian, Outaouais and Rideau sheep under conditions of an 8 month breeding cycle.

Borzan et al. (2015) carried out experiment aiming to evaluate the fertility, fecundity and prolificacy in order to compare some reproductive parameters between the Tsurcana breed and the Blanc du Massif Central rams crossed with Tsurcana ewes. In the batch of Tsurcana ewes mated with Blanc de Massif Central rams, the fecundity was 92%, the fertility was 88% and the prolificacy was 104%. Similar results we obtained in the control batch.

Rosa et al. (2007) compared the productive and reproductive performance of Romney Marsh (RM) and Merino Branco (MB) ewes in the Azores. In a preliminary trial, fertility, prolificacy and fecundity of 25 RM and 27 MB ewes were determined. In the second trial the reproductive indices (fertility: 96% versus 93%; prolificacy: 117% versus 140%; fecundity: 112% versus 130%) for RM and MB, respectively, were not significantly different. In conclusion the authors believe that MB appears to be a good alternative breed for exploitation in the Azores.

Fahmy (1986) studied the performance of 14 ewes from breed Romanovs imported from France and their progeny born in Canada over a period of five years are reported. Least-squares means for fertility were 100% for ewes mated in the fall and winter and 42% for those mated in May – June. Litter size at birth (2.86 ± 0.15) and at weaning (2.10 ± 0.15) were significantly affected by season of mating and parity. The most prolific matings were those of the fall (3.18) and of ewes in their 5th parity (3.54). The results showed that the Romanovs adapted well to the Canadian conditions.

Genetic characteristics

The prolificacy of sheep is determined by the litter size, and this factor is influenced by both the environmental and genetic factors. Conventional selection leads to slow progress, since the heritability of the trait is low (Morris, 1990). Of particular interest is the discovery of candidate genes (or mutations) with an effect on ovulation in sheep and litter size.

Many mutations have been found in genes expressing different proteins that influence on the fertility and ovulation rate in sheep (Barakat et al., 2017, Mulsant et al., 2001,

Wilson et al., 2001). According to Hanrahan et al. (2004) and Souza et al. (2001) there are three major fecundity genes – BMP1B or FecB (bone morphogenetic protein type 1B receptor – Booroola gene), GDF9 or FecG (growth differentiation factor 9) and BMP15 or FecX (bone morphogenetic protein 15). All three genes are from the family of Transforming Growth Factors- β (TGF- β), multifunctional proteins that regulate growth and differentiation in many cell types (Fabre et al., 2006, Knight and Glister, 2006). Members of this family play a major role during embryogenesis in mammals, amphibians and insects, as well as in bone development, wound healing, hematopoiesis, and some immune and inflammatory responses (Massague, 1998, Letterio & Roberts, 1998). TGF- β contains over 35 representatives, most of which have been shown to be involved in fecundity regulation processes.

The Booroola gene (FecB, BMP1B) is a single dominant autosomal gene and was first identified as a candidate fertility gene by Piper & Bindon (1982). It is also known as active in-like kinase 6 (ALK-6).

In sheep, FecB has a positive effect on ovulation and litter size (Piper et al., 1985, Piper & Bindon, 1996). Later studies found the localization of the gene in chromosome 6 and its correspondence to the equivalent in human chromosome 4q22-23 (Montgomery et al., 1993, 1994).

A review article by Abdoli et al. (2016) indicates that FecB has been successfully introduced as a genetic marker in breeding programs in many countries – Australia, Indonesia, China, India, England, New Zealand, France, Spain, Poland, Brazil .

Indigenous breeds are an important resource in which the genetic information is preserved, which at some point may be needed and valuable in the future. These breeds are characterized by high adaptability to unfavorable environmental conditions, but also they have significantly lower productivity compared to cultivated ones. Many authors have pointed out that the detection of genes with an effect on the productive and reproductive traits in sheep can have a positive effect on these traits and increase the cost-effectiveness. In supporting of this statement is the study of Yousif et al. (2013). The authors studied five indigenous Iranian breeds – Hamdani, Karadi, Awassi, Naeimi and Arabi – in which the polymorphism of the FecB gene locus was determined by PCR-RFLP method.

Using this method, Ghaffari et al. (2009) found genetic variation in locus of same gene in 239 sheep from another local Iranian breed, Shal sheep. This breed is mainly grown for meat. This breed is characterized by a high percentage of twinning, the average live weight for the rams is 82 kg and for the sheep – 61 kg. During the grazing period the animals have an average daily growth of about 250 g. The conclusion

of the authors of both studies is that due to its speed and accuracy, the PCR-RFLP method is suitable for the determination of single nucleotide polymorphisms in the FecB gene in sheep, but no mutant allele was observed in all genotyped animals. The published results are supported by Moradband et al. (2011).

Another study confirms that FecB increases fertility and can be applied in breeding as a genetic marker (Mahdavi et al., 2014). Kolehkoobi sheep homozygous for mutant BB allele and heterozygous B+ showed respectively 0.52 and 0.35 higher litter size, respectively, than homozygous non-mutant (wild-type) alleles ($P < 0.01$). No significant difference was found between animals carrying the mutant allele with heterozygous B+ and the homozygous BB genotype.

Genetic variation in FecB locus and its effect on fertility has also been studied in relation to improve the quality of semen characteristics in rams (Kumar et al., 2007). The authors found that the positive effect of the mutation discovered in ovogenesis was also observed in spermatogenesis.

Ghaffari et al. (2009) and Yousif et al. (2013) suggested that polygenic basis of the indicated quantitative trait (litter size), emphasizing the importance of extending the analysis by including results for genetic polymorphisms of other genes, such as FecG and BMP-15 in order to clarify the genetic basis of individual sheep prolificacy.

The second major candidate fecundity gene is **GDF9 or FecG**. It is an important growth factor that affects ovogenesis in most mammals (Su et al., 2004).

In sheep, GDF9 is found in chromosome 5 and eight different mutations (G1-G8) have been identified, three of them (G2, G3, and G5) leading to no change in gene expression (Hanrahan et al., 2004). The other five include nucleotide changes G1, G4, G6, G7 and G8 that lead to amino acid replacement. For example, the G1 mutation affects arginine at 87 bp in exon 1. According Hanrahan et al. (2004) expression of the protein is unlikely to change. Sheep with the heterozygous genotype of the GDF9 (FecGH) gene show decrease of fecundity (Hanrahan et al., 2004), whereas the animals with homozygous mutant genotype are infertile. This fact was also confirmed in the study of Chu et al. (2005), where animals with a homozygous genotype in mutant alleles have been reported to have anovulatory cycles, whereas in heterozygous animals the frequency of multiple ovulation is even higher.

Moradband et al. (2011) analyzed the variation in the locus of the FecG gene and the effectiveness of its influence on fertility in Baluchi sheep breed. The authors confirmed the work of Ghaffari et al. (2009) and Yousif et al. (2013) and concluded that the PCR-RFLP method is suitable for the determination of nucleotide polymorphisms in the sheep ge-

nome and indicated that the studied breed has a statistically significant effect of different GDF9 genotypes on the litter size ($P < 0.01$). Sheep with heterozygous FecG + / FecG1 and homozygous FecG1 / FecG1 genotype give 0.35 and 0.21 ($P < 0.05$) more lambs, respectively, than homozygous FecG1 / FecG1 genotype.

In another work Ghaderi et al. (2010) studied the polymorphism in GDF9 in two sheep breeds – Kordi sheep and Arabic sheep, which are characterized by high rates of twinning. Two specific restriction enzymes Hin6I and DdeI were used. The conclusion is that the first enzyme established genetic variation at the gene locus, while DdeI indicates that the populations are monomorphic. According to the authors, this provides information for development of future studies and the option of enzymes for the PCR-RFLP method.

The third major fecundity gene is **BMP15 or FecX** located on the X chromosome (Hanrahan et al., 2004). Moradband et al. (2011) indicate that 6 point mutations (FecXI, FecXH, FecXL, FecXG, FecXB, and a deletion of 17 bp from the coding region of the FecX gene in the Rasa Aragonesa breed) were identified in sheep at the BMP15 gene locus. Each of these has a significant effect on fecundity changing the gene expression

The deletion in the coding region of the BMP15 gene was described by Martinez-Royo et al. (2008). The authors analyzed a population of the Rasa Aragonesa sheep breed and found a deletion of 17 bp in the initial sequence of exon 2. This changed codon 154, shifting the reading frame and insert a new stop codon at position 208.

In three consecutive studies by Davis et al. (1991,1993) and Hanrahan et al. (2004) found that sterile sheep had two mutant alleles of the BMP15 gene (homozygous animals), whereas the heterozygous genotype (animals with one mutant allele) had a positive effect on ovulation and increased the twinning rate. The authors observed a positive effect on the ovulation and fecundity of both mutations at the loci of BMP15 and GDF9 (FecGH) genes when the animals had heterozygous genotypes, with an additive effect. This hypothesis is also supported in later studies by Gemmell N.J. & Slate J. (2006) and Martinez-Royo et al. (2008). The published results have shown that the highest fecundity animals have heterozygous genotypes of the BMP15 and GDF9 genes.

Studying the additive effect of mutant alleles at the loci of the three fecundity genes, collectively referred as Fec genes (Fecundity genes), Polley et al. (2010) analyzed the polymorphism at the loci of FecB, FecG and FecX genes in the Garole sheep breed. It is a local breed which, due to its high fertility and ability to adapt to environmental conditions, is widespread in India and is a major source of income for many farmers. The economic importance of the breed

substantiates the importance of genetic research. A total of 11 point mutations were detected in the three genes. The ARMS-PCR tetra-primer method was applied to FecX and FecG and 5 mutations were detected in each. Only one point mutation was observed at the FecB locus by the Touchdown PCR method. The authors conclude that the polymorphisms described at the loci of FecB and FecG genes in the Garole sheep breed have a significant effect on the fecundity of sheep. This requires more profound studies and including of more experimental animals

Conclusion

This review is indicative for the widespread use of DNA analysis in sheep breeding. The development of molecular technologies in recent decades has enabled reading of genome and detection of genetic markers for direct monitoring of polymorphic variation responsible for the phenotypic differences between individuals.

Marker assisted selection assists classical methods and can be performed at an early age by identifying the gene (s) determining the level of a certain productive trait. Improving reproductive performance in sheep is one of the key factors for increasing farm profitability. Selection by fecundity genes provides an opportunity to increase the efficiency of sheep farming. Results of the presented studies are unambiguous that more depth studies are needed to clarify the interaction between genes, which may modify their effects on the productive traits.

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