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***Review Article***

# GENETIC POLYMORPHISM OF PROLIFIC GENES IN GOAT - A BRIEF REVIEW

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**ABSTRACT: Animal geneticists' unvarying endeavor to maximize profit from livestock can be achieved by improving the genetic potential using appropriate selection methods. Genetic selection is an important tool for gaining maximum benefit from livestock. The improved reproductive efficiency and increased fertility rate of animal will ultimately pave the way for economic benefit of farmers. However, improvement of reproductive traits through selection is usually difficult to accomplish due to low heritability of traits. Therefore, immense efforts are being made to search some of major genes that would influence fecundity of animal. In this present context we focus on various SNPs of prolific genes associated with prolificacy in goat.**

**Key words**: Fertility, Fecundity, Gene, Goat, Prolificacy.

## INTRODUCTION

The conventional breeding program is primarily focused to improve the production performance of livestock to meet the growing demand of population. However, selection only for production traits will lead to declination of many fitness traits due to negative genetic correlation (Mishra 2014). Consequently, a simultaneous improvement of production as well as reproduction traits is an utmost necessary in breeding program. Improvement of reproductive traits of any domestic species including small ruminants is the key interest of animal breeders' community as moderate increase in litter size can lead to outsized profit.

However, the reproductive traits are mostly sex limited having low heritability values and are expressed in later part of life. In addition, the lack of knowledge on the number of the genes controlling these traits and the possible gene interactions are the other precincts. Hence, traditional selection method proved not so efficient for effective genetic improvement of reproductive traits.

### Genes responsible for fecundity in goat

Molecular genetics can overcome the limitation of traditional selection method for the improvement of reproductive traits, as it analyzes the genetic variability directly at the DNA level. A number of genes controlling prolificacy in goat have been reported earlier (Table 1). Despite the progress made in goat fecundity studies, it is hard to satisfy the actual application because the reproductive traits are complex quantitative traits involving multiple genes, loci and interactions (Ahlawat *et al*. 2015a). So it is important to analyze the combined effect of multiple genes simultaneously (Tudu *et al*. 2015, Ray *et al*. 2016).

### Bone Morphogenetic Protein 15 (BMP15)

BMP, the oocyte-secreted protein is the largest subgroup of the transforming growth factor - ß (TGF- ß) super family (Shimasaki *et al*. 2004). The BMP15, an X linked gene, is also known as *FecX* (Galloway *et al*. 2000) that stimulates follicle growth, granulosa cell proliferation and cell-survival signaling by promoting mitosis and suppressing FSH receptor expression (Moore *et al*. 2003). Genetic polymorphisms (FecXI, FecXH, FecXB, FecXG, FecXL and FecXR) of the BMP15 gene were reported to be associated with increased ovulation rate and litter size in sheep (Juengel *et al*. 2002, Juengel *et al*. 2003, Bodin *et al*. 2007, Martinez-Royo *et al*. 2009).

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However, any such polymorphism (*FecB* and *FecX* loci of BMP15 reported in sheep) could not be identified in Indian (Marwari), Chinese and Iranian (Markhoz) goat breeds (Godara *et al*. 2012, He *et al*. 2010). The FecXB mutation was found to be associated with triplets in Guizhou goat population (Lin *et al*. 2007). Ovulation rates in BMP15 mutants are high in the heterozygote while the homozygous mutants show a primary ovarian failure resulting in complete sterility (Galloway *et al*. 2000, Bodin *et al*. 2007, Monteagudo *et al*. 2009). The reason may be due to negative genetic effect of homozygotes on ovulation.

The polymorphic sites have been published for exon 2 of BMP15 gene in Jining Grey goats and White goat population of China (Chu *et al*. 2007, Ran *et al*. 2009). The comparative nucleotide sequence analysis of BMP15 gene among Indian and exotic goats (Jining Grey goat) revealed single transition in exon 1, two transitions and one transversion in exon 2. The A898G mutation in Jining Gray goat is responsible for Ser32Gly change in mature peptide of BMP15 gene and the allele G was found to be associated with higher litter size. The Ser32Gly mutation was predicted to alter the binding of BMP15 with receptor (Feng *et al*. 2014). Two novel SNPs (G735A and C808G) were observed in exon 2 of the BMP15 gene with no evidence of being related to litter size in Indian goat breeds. The BMP15 gene was found to be polymorphic for exon 2 both in high fecundity Funiu white goat and low fecundity Taihang black goat (Wang *et al*. 2011a).

**Growth Differentiation Factor 9 (GDF9)**

Initially the GDF9 was identified as an oocyte-derived growth factor required for ovarian somatic cell function. GDF9 increases the number of primary follicles with a subsequent decrease in the number of primordial follicles (Vitt *et al*. 2000). Earlier study could not reveal any polymorphism in GDF9 gene of Black Bengal goat (Polley *et al*. 2009). But three non-synonymous SNPs (C818T, A959C and G1189A) were subsequently identified in exon 2 among indigenous goat breeds. Four SNPs (G3288A in intron 1, G423A, A959C and G1189A in exon 2 associated with prolificacy were detected in four different goat breeds of China. One of these alleles (A959C) showed significant correlation with higher litter size in Jining Grey goats. The nucleotide sequence of GDF9 gene of Indian goats was compared with exotic goat (Jining grey goat, EF446168) where 2 transversions (A1962C, G2254T) were identified in exon 1 and flanking region whereas 3 transitions (T3623C, C3722T and G4093A) and 1 transversion (A3863C) were observed in exon 2 (Ahlawat *et al*. 2012). The polymorphism of GDF9 gene was investigated in three goat breeds (Xinong Saanen, Guanzhong and Boer) and one allelic variant (G4093A) was found to have significant effect on litter size (An *et al*. 2012). The relationship between the genetic polymorphism of GDF9 gene and the litter size was investigated in five breeds of black goats *viz*. Big foot black goats, Jintang black goats, Hainan black goats, Guizhou black goats and Taihang black goats (Zhu *et al*. 2013). A single nucleotide mutation (A792G) in exon 2 of GDF9 gene in Big foot black goats and Jintang black goats was observed.

**Bone Morphogenetic Protein Receptor 1B (BMPR1B)**

The booroola fecundity gene *i.e*. BMPR1B (FecB) plays an important role for increase in ovulation rate and litter size. Most of the researches on BMPR1B gene have been focused on identifying the presence of single point mutation (A746G) *i.e*. FecB mutation of the coding region in the BMPR1B gene causing an amino acid change (Q249R) which is associated with the hyper prolific phenotype of Booroola ewes (Souza *et al*. 2001). Though, similar polymorphism could not be identified in some goat breeds of India, China and Thailand (Hua *et al*. 2008 and He *et al*. 2010), the BMPR1B gene was found to be polymorphic in Black Bengal goats (Polley *et al*. 2009). The polymorphism study in the promoter and exonic regions (exon 1, 2 and 6 to 9) of BMPR1B gene in 8 indigenous goat breeds (Barbari, Beetal, Black Bengal,

**Table 1. Genomic distribution of major genes affecting prolificacy in goat.**

| Gene | Chromosomal Location | Length of CDS | No. of Exons | Accession No. |
|---|---|---|---|---|
| BMPR1B | 7 | 1509 | 2 | NC_022299 |
| BMP15 | 11 | 1182 | 2 | NC_000023.10 |
| GDF9 | 7 | 1362 | 2 | NC_022299.1 |
| POU1F1 | 1 | 876 | 6 | NC_022293.1 |
| PRLR | 20 | 1806 | 9 | NC_022312.1 |
| FSHR | 11 | 2010 | 10 | NC_022303.1 |
| KISS1 | 16 | 408 | 3 | AB433789/ NC-022308.1 |
| GPR54 | 7 | 1137 | 6 | GU142846/ NC-022307.1 |
| Inhibin HA | 2 | 996 | 2 | NC_022294 |
| BMP4 | 10 | 1230 | 4 | NC_022302 |
| IGF1 | 5 | 465 | 4 | NC_022297 |
| GH | 19 | 564 | 4 | NC_022311 |
| GHR | 20 | 1938 | 10 | NC_022312 |
| ESR1 | 9 | 1611 | 9 | NC_022301.1 |
| ESR2 | 10 | 1818 | 8 | NC_022302.1 |
| FSHB | 15 | 390 | 3 | NC_022307.1 |

Malabari, Jakhrana, Osmanabadi, Sirohi and Ganjam) revealed two novel SNPs T(-242)C and G(-623)A in the caprine BMPR1B promoter region (Ahlawat *et al*. 2013a). Similarly, four variations, one each in exon 6 (G674A), exon 7 (G1053A), exon 8 (C1253T) and exon 9 (C1367T) were observed in Indian goat as compared to Jining Grey goat of China (Ahlawat *et al*. 2013b). All the nucleotide variations were synonymous thus no change is expected in the amino acid sequence.

**Bone Morphogenetic Protein 4 (BMP4)**

During embryonic development BMP4 helps in mesoderm induction, endothelial progenitor differentiation, ectoderm differentiation and myogenic induction (Sasai and Robertis 1997, Dale and Jons 1999). BMP4 plays a crucial role in follicular growth and differentiation, cumulus growth and ovulation (Onagbesan *et al*. 2003, Shimasaki *et al*. 2003).

Two SNPs (A1986G, G2203A) in intron 2 and one microsatellite polymorphism (CA dinucleotide repeat) were identified in BMP4 gene of four goat breeds. The microsatellite located in the 30 flanking region near the termination site of coding region of BMP4 can act as a potential DNA marker to improve the litter size in goat (Chu 2011). Polymorphism study in nine Indian goat breeds (Barbari, Beetal, Black Bengal, Malabari, Jakhrana, Osmanabadi, Sangamneri, Sirohi and Ganjam) revealed a non-synonymous SNP (G1534A) in exon 2 causing amino acid change from arginine to lysine (Sharma *et al*. 2013).

**Follicle Stimulating Hormone Receptor (FSHR)**

The FSHR found exclusively on granulosa cells, is a member of the rhodopsin receptor family of G protein coupled receptors. The FSH-FSHR system relays neuronal signals from the hypothalamus to the gonads and induces feedback signals to the hypothalamus and pituitary. This keeps the endocrine balance in the reproductive axis and maintains follicle growth, development, differentiation and maturation as well as spermatogenesis. An increase in the level of FSHR mRNA as well as its alternative splicing appears to be important during early folliculogenesis.

In Yunling Black and Boer goats, 4 mutations *i.e.* A486C (Arg162Ser), C1042G (Pro348Ala), T1930A (Phe644Ile) and T2036C (Thr679Ile) were identified in the coding region of the FSHR (Guo *et al*. 2013). The polymorphism in 5' regulatory region (G739GT in Boer goats and -C93CA, -G80C, -C63A, -C56G, and -T55C in Xiangdong Black, Nanjiang Brown, and Guizhou Black goats) of the caprine FSHR gene was also identified (Song *et al*. 2006, Zhu *et al*. 2007). In the 5' regulatory region of the FSHR gene, 2 novel mutations (T26A and A61C) in Boer goats and another 2 novel mutations (T70A and G130C) in Jining Grey, Inner Mongolia Cashmere, and Boer goats were also reported (Guo *et al*. 2013). All the above mentioned mutations were found to be associated with litter size in goats.

**Growth Hormone (GH)**

The growth hormone of mammals plays an important role in the female reproduction controlling cell division, ovarian folliculogenesis, oogenesis and secretory activity (Schams *et al*. 1999, Hull and Harvey 2002, Ola *et al*. 2008). The goat growth hormone gene is duplicated (Kioka *et al*. 1989), one of the copies codes for pituitary GH and the other one is expressed in the placenta. Thus it has implications both in pre-natal as well as postnatal growth (Supakorn 2009). Two SNPs (A781G and A1575G) in exon 2 of GH gene were found to have significant effect on litter size in Boer and Matou goats (Zhang *et al*. 2011).

**Gonadotropin Releasing Hormone Receptor (GnRHR)**

The GnRHR is a member of the rhodopsin-like G protein coupled receptor (GPCR) family (Stojilkovic *et al*. 1994) that triggers the synthesis and release of the LH and FSH, the key regulators of the production of gametes and gonadal hormones (Naor 2009). Polymorphism of GnRHR gene in Saanen Dairy Goat and the litter size trait was ascertained (Han *et al*. 2009). Two novel SNPs in exon 1 of GnRHR gene were found to have significant association with litter size in Xinong Saanen Dairy goat and Boer goat (An *et al*. 2009). Two SNPs (G891T and G757A) were found in the exon 1 of the GnRHR gene was found to have significant effect on litter size in Boer goat (Yang *et al*. 2011). Three SNPs (A730G, G757A and G891T) were identified in the local nondscriptive goat population of Sri Lanka (Ariyarathne *et al*. 2015). The first two SNPs (A730G, G757A) were silent and the other one (G891T) is responsible for amino acid (Arg/Met). Relationship between the polymorphism of GnRHR gene and litter size in Chuandong White goat, Gulin Ma goat and Guizhou White goat was determined (Huang *et al*. 2012). One mutation (G154A) was found to have higher litter size. Iraqi goats with mutation (A177T) of exon 2 GnRHR gene was found to be associated with litter size (Li *et al*. 2011, Taklan *et al*. 2015).

**Prolactin Receptor (PRLR)**

The prolactin is an anterior pituitary peptide hormone which mediates its action by its receptor (PRLR) present in various organs like brain, ovary, placenta and uterus (Tzeng and Linzer 1997, Cassy *et al*. 1998). The PRLR

**Table 2. Single Nucleotide Polymorphisms (SNPs) in fecundity related genes of goat.**

| Gene | Synonymous Nucleotide | Variation | Non-synonymous Nucleotide | Variation | Gene | Synonymous Nucleotide | Variation | Non-synonymous Nucleotide | Variation |
|---|---|---|---|---|---|---|---|---|---|
| BMP15 | rs63649212 | C/T | rs645296495 | C/G | POU1F1 | rs641347841 | A/G | rs647935675 | C/G |
| | rs637982942 | C/T | rs660780901 | A/G | | rs642436119 | C/T | rs653591908 | C/T |
| | rs652783379 | A/C | | | | rs644431821 | A/G | rs654784175 | A/C |
| | rs653750770 | A/G | | | | rs650043961 | C/T | rs655316948 | C/G |
| | rs650650729 | C/T | | | | rs664446549 | A/G | | |
| GDF9 | rs651511232 | A/C | rs637044681 | C/T | | rs66666022 | C/T | | |
| | rs669811820 | G/T | rs637835524 | A/G | | rs667991361 | A/G | | |
| | | | rs645345606 | G/T | | rs670830003 | A/C | | |
| | | | rs654628150 | C/G | BMP4 | | | rs643790179 | A/G |
| | | | rs662668357 | A/G | | | | rs653978326 | A/G |
| | | | rs666975374 | C/G | IGF1 | rs644667813 | C/T | rs655800693 | G/T |
| | | | rs671913497 | C/G | | rs660893782 | C/T | rs665890236 | A/G |
| ESR1 | rs636140215 | A/T | | | GH | rs642772288 | A/G | rs654241917 | C/T |
| | rs638885803 | C/T | | | | rs652793888 | A/G | | |
| | rs640391300 | C/T | | | | rs668836605 | C/T | | |
| | rs64431751 | C/T | | | GHR | rs635600272 | A/G | rs637070147 | A/G |
| | rs645280330 | C/T | | | | rs652082852 | C/T | rs638447274 | C/T |
| | rs648268132 | G/T | | | | rs654819245 | A/G | rs648681395 | G/T |
| ESR2 | rs639396396 | A/G | rs663461902 | A/C | | rs658866479 | C/T | rs655681726 | A/G |
| | rs63966175 | A/G | rs663723690 | A/G | | rs668880480 | A/G | rs656064959 | A/C |
| | rs644688731 | C/T | rs664723883 | C/T | | rs671333290 | G/T | rs662251196 | C/T |
| | rs650592134 | C/T | | | | | | rs672506459 | C/T |
| | rs656509774 | A/G | | | FSHR | rs640541332 | C/T | rs636492691 | C/T |
| | rs658618681 | A/G | | | | rs645810960 | A/G | rs636667991 | C/G |
| | rs660969973 | A/G | | | | rs646701326 | A/G | rs639539138 | C/T |
| | rs663137561 | A/G | | | | rs648076133 | A/G | rs640490222 | C/T |
| FSHR | rs649021945 | A/G | rs648313982 | C/T | ADAM22 | rs641554574 | A/G | rs639022017 | A/G |
| | rs667125751 | A/G | rs655554603 | C/T | | rs643652765 | C/T | rs639075740 | C/T |
| | | | rs661835998 | A/G | | rs655703738 | A/G | rs656345255 | C/G |
| | | | rs670772500 | A/T | | rs659208517 | A/G | rs657412245 | A/G |
| | | | rs670940245 | C/T | | rs66059486 | C/T | rs658558182 | C/T |
| PRLR | rs647561406 | C/T | rs643693943 | A/G | | rs663252350 | A/G | rs662748783 | C/T |
| | rS648738199 | C/T | rs644025319 | A/G | | rs665133119 | A/G | rs665216067 | A/G |
| | rs6505295 | C/T | rs644916131 | A/G | SYCP1 | rs640281782 | A/G | rs637593985 | C/T |
| | rs6547118481 | C/T | rs650808841 | A/G | | rs643531138 | C/T | rs638745973 | C/G |
| | rs662230359 | A/G | rs658600886 | A/G | | rs644118237 | C/G | rs639035219 | G/T |
| | rs670217350 | C/T | rs661858392 | A/G | | rs644391917 | C/T | rs641644020 | C/G |
| | | | rs666447698 | A/G | | rs645400495 | A/G | rs640840801 | C/T |
| | | | rs668650719 | G/T | | rs645816540 | C/T | rs643391824 | C/T |
| | | | rs668940651 | A/G | | rs661807611 | C/T | rs644661738 | C/T |
| SRD5A2 | rs640070414 | A/G | | | | rs662658643 | C/T | rs650268370 | C/T |
| | rs645884147 | A/G | | | | rs663680964 | C/T | rs650577017 | C/T |
| | rs658279990 | C/T | | | | rs665396150 | C/T | rs652859218 | C/G |
| | rs660306059 | A/G | | | | rs665989288 | C/T | rs653921270 | A/G |
| | rs670553742 | G/T | | | | | | rs659504757 | C/T |
| | rs671232679 | C/T | | | | | | rs659869862 | C/G |
| NMU | rs648350930 | C/T | rs638540857 | A/G | | | | rs664306550 | A/T |
| | | | rs649477577 | C/T | | | | rs665726686 | A/T |
| | | | rs649936050 | A/G | | | | rs671187186 | G/T |
| | | | | | | | | rs671426233 | C/T |

gene is a member of the growth hormone/prolactin receptor gene family containing regions of identical sequences (Kelly *et al*. 1991). The prolactin and growth hormone receptors are homologous to receptors for members of the cytokine super family (Clevenger *et al*. 1998). Polymorphism in intron 1 and intron 2 of PRLR gene were detected in high prolificacy (Jining Grey) and low prolificacy (Boer, Wendeng dairy, Liaoning Cashmere and Beijing) goats (Di *et al*. 2011). However, genetic variation in intron 1 has no significant influence on litter size but intron 2 has significant effect on litter size in goat (Li *et al*. 2010). The mutations in exon 10 of PRLR gene was predicted to be associated with the reproductive effects of high fecundity Chinese Lezhi black goat (Wu *et al*. 2013).

**Inhibin**

Inhibin is a glycoprotein gonadal hormone, which can inhibit the synthesis and secretion of FSH (Robertson *et al*. 1985, Woodruff *et al*. 1996). It has 2 subunits, ∝ and β, linked by disulphide bonds. Two inhibins, sharing a common ∝-subunit but different β-subunits (βA or βB) have been identified (Mason *et al*. 1985). A missense mutation of INH∝ gene has an important role in receptor binding and has been indicated in premature ovarian failure. The inhibin-βB (INHBB) gene with a mutation (A782G) in its exon 2 was reported to be associated with the prolificacy in Jining Grey goats (Chu *et al*. 2012). The above polymorphism could not be identified in any of the nine different goat breeds of India as favourable 'A' allele was fixed (Sharma *et al*. 2015). However, two synonymous novel SNPs (G693A and C840T) without causing any change in amino acids were identified in Indian goat populations.

**Insulin like Growth factor 1 (IGF1)**

The IGF1 has an important role in reproduction, foetal development and growth (Sirotkin *et al*. 2003, Velazquez *et al*. 2008,Wang *et al*. 2011b). It regulates the secretion of gonadotrophin releasing hormone, stimulates ovarian function and steroidogenesis (Djuricic *et al*. 2011) likely due to anti-apoptotic effects (Yu *et al*. 2003). IGF1 also mediates the nutritional effects on the follicular development (Webb *et al*. 2004, Mangalhaes 2012) and the first postpartum ovulation.

Two SNPs (G224A and T227C) in IGF1 gene were found to be associated with litter size in Malabari and Attappady Black goat (Thomas *et al*. 2016). Similarly the polymorphisms (A1637G, T1640C) in 5′ flanking region of IGF1 gene seemed to affect the litter size in Gulin Ma goats (Wang *et al*. 2011b). The SNP (G1617A) in IGF1 gene of Iranian Markhoz goat has shown to have significant association with litter size.

**Kit Ligand (KITLG)**

Kit ligand encoded by the KITLG (also known as the steel) gene is expressed in follicles at all stages of development (Yoshida *et al*. 1997). KL/c-Kit system, in goat ovaries, is involved in the regulation of folliculogenesis and luteal activity (Silva *et al*. 2006). The identified three SNPs (T769C and G817T and G9760C) in KITLG gene of Xinong Saanen, Guanzhong and Boer goat breeds were significantly associated with litter size (An *et al*. 2012).

**Melatonin Receptor**

Melatonin hormone is produced rhythmically by the pineal gland (von Gall *et al*. 2002) and targets two high-affinity G protein-coupled receptors *viz*. melatonin receptor 1A (MT1) encoded by MTNR1A and MT2 encoded by MTNR1B (Dubocovich *et al*. 2010). However, any polymorphism could not be identified in the exon 2 of MT2 gene in goat (Jia *et al*. 2012).

**Cocaine Amphetamine Regulated Transcript (CART)**

The CART is a candidate gene in the hypothalamic-pituitary-gonadal axis and hypothalamic-pituitary-adrenal axis, particularly in the regulation of GnRH secretion (Boone *et al*. 2008). The polymorphisms study of the CART gene in ten goat breeds revealed ten novel SNPs and three microsatellites. The intronic mutation (C524A) of CART gene had significant effect on litter size in three Chinese goat breeds *i.e*. Chuandong White, Guizhou White and Gulin Ma (Wang *et al*. 2011c).

**Kisspeptin (KISS1)**

Kisspeptin, the product of the KISS1 gene, is a hypothalamic neuropeptide that impacts fertility by stimulating gonadotropin-releasing hormone (GnRH) neurons (Gottsch *et al*. 2004). The KISS1 gene was originally identified as a human metastasis suppressor gene (Lee *et al*. 1996) operating via G-protein coupled receptor GPR54. The GPR54 (also known as KISS1R) is a major upstream regulator of neurons secreting GnRH. The polymorphism of KISS1 gene was found to have relationship with high prolific and sexual precocity in goats (Othman *et al*. 2015). Out of the eleven SNPs of KISS1 gene identified in three goat breeds, four SNPs (G384A, T2849C, G2510A and C2540T) were found to be associated with litter size (An *et al*. 2013a). A particular genotype *viz*. AATTAATT and TTAATT of SN breed and BG breed of goat, respectively had higher litter size than other genotypes. Two SNPs (T2124A and C2270T) in the KISS1 promoter region were found to be significantly associated with litter size in three goat breeds (An *et al*.

2013b). In nine Indian goat breeds, nine SNPs were identified in intron 1 (G296C, T455G, T505A, T693C and T950C) and intron 2 (T1125C, A2510G, C2540T and A2803G). Out of them G296C, A2510G and C2540T polymorphism were found to be associated with litter size (Maitra 2014a). A functional analysis of SNP (G1384A) in KISS1 promoter region was found to be associated with litter size in the Guanzhong goats (An *et al*. 2015). Three polymorphisms were detected in KISS1 gene for Black Bengal goat breed by PCR-RFLP which was predicted to have role in litter size (Gupta *et al*. 2015). The SNP (T2643C) and 8_bp base deletions (2677 AGTTCCCC) in intron 2 of the goat KISS1 gene was found to have significant effect on litter size (Hou *et al*. 2011).

**GPR54/KISS1R**

The *GPRR54* (also known as AXOR12, KiSS1R, KiSS-1/GPR54) is a regulator of puberty and Kisspeptin acts as its ligand (Roa *et al*. 2008). The three SNPs (G4014A, G4136A and C4152T) in exon 5 were reported to have some correlation with sexual precocity in goats (Cao *et al*. 2011). Two novel SNPs (C1122T in exon 1 and T1830C in intron 1) were reported in Indian goats (Maitra *et al*. 2014b). The two SNPs (C1122T in exon 1 and C4152T in exon 5) were reported to have correlated with litter size in goat (Cao *et al*. 2011, Ahlawat *et al*. 2015b).

**Pituitary transcription factor-1 (POU1F1)**

POUIF1 (also named PIT-1 or GHF-1) is mainly expressed in the pituitary gland and plays an important role in the expression of GH, prolactin and thyroid stimulating hormone β (TSH-β) in mammals (Wollard *et al*. 2000). Accordingly, mutations on this gene possibly result in deficiency of GH, PRL and TSH (Cohen *et al*. 1997, Li *et al*. 1990). Six mutations *i.e*. C256T in exon 3, C53T and T123G in intron 3, and G682T (A228S), T723G and C837T in exon 6 were identified in caprine POU1F1 gene. Out of them C256T and G682T SNPs were reported to be associated with litter size (Feng *et al*. 2012).

**Genetic variation among fecundity related genes of goat**

The genetic variation is the primary cause of differential expression of genotype. The SNP is the most important source of genetic variation in animals due to their abundance in nature. The effect of SNPs can also be predicted as a change in amino acid sequence consequently modification of protein structure and function. Therefore, the available SNPs in public database of fecundity related genes in goat are summarized (Table 2).

**CONCLUSION**

Identification of various genetic polymorphisms (SNPs) and their association with prolificacy may be helpful for enhancing the reproductive efficiency among different goat breeds. Since reproductive traits are polygenic in nature and controlled by many genes, identification of all the available genetic variations of the population will help to carry out marker assisted selection in a more precise manner. The BMPR1B, BMP15, GDF9, KISS1, GPR54, GHR genes with multiple SNPs may be suitable candidate genes for increasing the litter size in goat.

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