Indian Journal of Animal Sciences **91** (5): 327–336, May 2021/Review Article
https://doi.org/10.56093/ijans.v91i5.115380

Impact of Booroola fecundity gene introgression on sheep production: Indian perspective

ARUN KUMAR[1], RAJIV KUMAR[1], S S MISRA[1] and R C SHARMA[1]

ICAR-Central Sheep and Wool Research Institute, Avikanagar, Rajasthan 304 501 India

Received: 15 July 2021; Accepted: 21 July 2021

ABSTRACT

Surge of demand for meat from diverse sources in a time of decling land and other natural resources shifted the trend of producing more sheep per sheep. Prolificacy aspect in sheep can be used as an important arsenal to fulfil this objective. *FecB* gene mutation perhaps spread from Garole microsheep of India, has been widely used for introduction of prolificacy in monotocus sheep worldwide. The ovulation rate and litter size are two most important reproductive parameters influenced by *FecB* gene besides small influences on other sheep production parameters. While implementing the *FecB* introgression programmes precaution needs to be observed to avoid lamb mortality. The results of the experiments conducted worldwide on *Fec*B introgression programmes suggest that high prolificacy is economically beneficial under intensive and semi-intensive management system of sheep rearing. There were variable effects of *Fec*B genotype documented from different parts of the world. With goal oriented research efforts, the prolificacy in *FecB* carrier Avishaan sheep, a triple breed cross developed from Garole, Malpura and Patanwadi at ICAR-CSWRI are showing promising sheep for future. There are several challenges for using *Fec*B gene in the future using assisted reproductive and genome editing technology. The effect of *FecB* gene on different sheep production parameters as reported in the literature are summarized in present work.

Keywords: *FecB gene*, Lamb survivability, Litter size, Ovulation rate, Prolificacy, Sheep

Growing human population is exerting tremendous pressure on surging demand of food from different sources. As a consequence, demand for animal protein, particularly meat is also growing with rapid pace. Due to constraint in natural resources like available grazing land, feed and fodder resources, trend is shifting towards producing more sheep per sheep. Prolificacy can be used as an important arsenal to fulfil this objective. Identification and utilisation of the major genes for prolificacy in sheep has been gaining pace since 1980s (Davis *et al.* 1982). The major genes for fecundity affecting ovulation rate and litter size have been documented in merino sheep breed named the *Fec*B by the committee on genetic nomenclature of sheep and goats (Singh *et al.* 2009). The origin of the Booroola Merino can be traced back to the prolific dwarf Garole sheep that were introduced into Australia in the late 18th century (Davis *et al.* 2002). After the discovery of *FecB* gene in Australian Booroola Merinos (Wilson *et al.* 2001), *FecB* gene was identified in Garole (Davis *et al.* 2002) and Kendrapada sheep (Kumar *et al.* 2008a) from India, Javanese (Davis *et al.* 2002) from Indonesia, Hu and Small Tailed Han breeds from China (Davis *et al.* 2006) and Kalehkoohi sheep of Iran (Mahdavi *et al.* 2014). Most of the spread of *FecB* to other breeds worldwide has resulted from crossbreeding with the *FecB* gene carrier breeds during the last 40 years, using either rams or artificial insemination. The Booroola fecundity gene was first identified on the basis of segregational studies on litter size (Piper and Bindon 1982) and ovulation rate (Davis *et al.* 1982). It was found that Booroola phenotype showed a Mendelian pattern of segregation. The Booroola gene (*FecB*) is a dominant autosomal gene, which is having an additive effect on ovulation rate (Piper *et al.* 1985). The *FecB* locus is situated in the region of ovine chromosome 6q$^{23-31}$, which is syntenic to the region of human chromosome 4q$^{21-25}$ (Montgomery *et al.* 1993, 1994). The high prolificacy in Booroola Merinos is due to the mutation at the 830 nucleotide position (A to G transition) leading to a change from glutamine to an arginine (Q249R) in a highly conserved intracellular kinase signaling domain of the bone morphogenetic protein receptor 1 B (BMPR1B), which is expressed in the oocytes and granulosa cells (Mulsant *et al.* 2001, Souza *et al.* 2001, Wilson *et al.* 2001). Sheep carrier for *FecB* mutation produces twins and triplets in one lambing. Due to the *FecB* mutation, BMPR1B would be inactivated partially leading to an advanced differentiation of granulosa cells and an advanced maturation of ovulatory follicles (Mulsant *et al.* 2001). It was observed that *FecB* mutation might alter the interaction of bone morphogenetic proteins (BMPs) molecules with other factors regulating FSH secretion *in vivo* (Young *et*

Present address: [1]ICAR-Central Sheep and Wool Research Institute, Avikanagar, Rajasthan. ✉Corresponding author email: karunt04@yahoo.com

al. 2008). Presently, how *FecB* mutation affecting the secretion of progesterone, FSH and ovulation rate is not exactly unravelled.

After the discovery of the *FecB* mutation, there has been increasing interest in identification and utilization of the *FecB* mutation in improving the prolificacy of non-prolific sheep breeds worldwide. Initially *Fec*B carrier sheep were segregated based on ovulation rate and size of ovulating follicles (Davis *et al.* 1982). DNA tests based on microsatellite markers were developed which was able to detect *Fec*B carrier status with 90% accuracy (Montgomery *et al.* 1993). Later on forced PCR-RFLP test was developed (Wilson *et al.* 2001, Davis *et al.* 2002) for accurate detection of *Fec*B mutation. Thus, *FecB* introgression programs were rapidly applied in several countries and the results of these programs improved the litter size and prolificacy of the monotocus sheep breeds. Many aspects of the *FecB* gene including body weight, litter size, ovulation rate, fertility, lamb survival, milk, meat, wool and other traits have been studied in *FecB* carrying sheep breeds or strains all over the world.

Effect of FecB *Introgrssion on sheep production*

There were variable effects of *Fec*B introgression programmes documented from different parts of the world. The effect on various sheep production traits/parameters as reported in the literature are discussed below and summarized in Table 1.

Ovulation rate and litter size: The ovulation rate and litter size are two most important reproductive parameter influenced by introgression of *FecB* gene. In Australia and New Zealand, pioneering works were started in 1980s, where Booroola merino ewe possesing *FecB* gene had crossed with Border Leicester, Dorset horn and other local sheep. These works had reported an increase in ovulation rate and litter size in *FecB* carrier ewes (Piper *et al.* 1985, Davis *et al.* 1991, Piper and Bindon 1996). The effect of *FecB* gene was additive for ovulation rate and each copy of the *FecB* gene increased ovulation rate by about 1.6 and the effect of single and two copy of the *FecB* gene on litter size was reported as 1.0 and 1.5 in Booroola Merino, respectively (Davis *et al.* 1991, Davis 2004). Similarly, one copy of *FecB* gene had increased ovulation rate by about 1.3 and litter size by 0.9-1.0 in Javanese thin tail sheep from Indonesia (Bradford *et al.* 1986). In Israel, Awassi and Assaf sheep were producing 1.2 and 1.6 lambs per ewe lambing, respectively (Epstein 1985). *FecB* introgression from Booroola Merino rams had increased the lambing about 2.0 lambs per ewe and the single copy of the *FecB* gene had increased lambing by about 0.67 extra lambs (Gootwine *et al.* 1995). By 2003, the prolificacy of the Assaf ewes carrying one or two copies of the *FecB* gene was increased to 2.44 and 2.55 lambs per lambing, respectively (Gootwine *et al.* 2003). Study in France had reported 0.9 extra lambs with single copy of *FecB* gene in Merino d'Arles-cross ewes (Teyssier *et al.* 1998). Similar study in the United States of America, single copy of *FecB* gene had reported 0.65 extra lambs in Booroola Merino-Rambouillet crossbred ewes (Southey *et al.* 2002). The two copy of the *FecB* gene had increased the litter size about 3.0 and 2.9 in Chinese Hu and small tail Han sheep, respectively (Davis *et al.* 2006). In another study in Chinese small tail Han documented 1.40 and 1.11 more lambs with double and single copy of *FecB* gene, respectively as compared with non-carrier ewes (Chu *et al.* 2007). In Chinese prolific meat strain, two copy of the *FecB* gene had increased the litter size by 2.84 (Guan *et al.* 2007). Recently, the effect of *FecB* gene in litter size in Chinese sheep breeds had been analyzed with similar findings (Chong *et al.* 2019). In India, NARI, Phaltan, Maharastra had started introgressing *FecB* gene from Garole into monotoccus Deccani and Bannur sheep. The study reported that single copy of the *FecB* gene had increased litter size from 1.53 to 2.03 in Deccani or Bannur crosses (Nimbkar *et al.* 2003). Furthermore there had been an increase in ovulation rate from 1.03 (non carrier) to 2.03 and 3.37 in single and double copy *FecB* gene carrier Deccani or Bannur ewes (Pardeshi 2008).In other study, single copy of the *FecB* gene had increased the litter size of 0.93 in Garole × Malpura ewes (Kumar *et al.* 2006). Further it was reported that single and two copy of the *FecB* gene increases 0.70 and 1.14 extra lambs in Garole × Malpura sheep (Kumar *et al.* 2008b). Based on above studies, it can be affirmed that the *FecB* gene increases the ovulation rate and litter size as compared with non carrier ewes.

Fertility: The low increment in litter size as compared to ovulation rate for *FecB* carrier ewes was speculated that *FecB* gene reduces fertilization rate and/or embryo survival. It was observed that embryo mortality increases with the ovulation rate (Hanrahan 1980). The fertilization failure was found higher in *FecB* carrier ewes as compared to *FecB* non-carrier ewes (Kleemann *et al.* 1990). In another study, it was also revealed that the Booroola Merino × Dorset heterozygous ewes had lower fertility than the non-carrier ewes (Fogarty *et al.* 1992). There was significant increase in non-pregnant in double copy *FecB* (16.4%) ewes as compared to single copy *FecB* (7.6%) and non carrier (4.1%) ewes (Farquhar *et al.* 2006). Low fertility in Booroola ewes (0.88) had also been observed as compared to control Merino ewes (0.92) in another study (Walkden-Brown *et al.* 2009). In contrast, no difference in the fertility between the *Fec*B carrier and *FecB* non carrier ewes within the same genetic background had been reported (Meyer *et al.* 1994, Southey *et al.* 2002). Similarly, the *FecB* genotype did not affect the fertility of Booroola-Rambouillet ewes (Schulze *et al.* 2003). Newer insights into the functional significance of *FecB* gene in the male reproductive system are emerging (Shimasaki *et al.* 2004). The effect of the *FecB* gene on semen production and sperm motion characteristics was studied in Garole × Malpura rams (Kumar *et al.* 2007). The results indicated an effect on sperm concentration which was slightly higher in *FecB* carrier rams as compared with *FecB* non-carrier rams. Previous studies had found that the *FecB* gene increases FSH concentration in adult rams after

Table 1. Effects of *FecB* introgression on different sheep production parameters

Trait	Sheep breed/strain	Country	*FecB* genotype			Reference
			FecB ^{BB}	*FecB* $^{B+}$	*FecB* $^{++}$	
Ovulation rate	Javanese thin tailed	Indonesia	–	2.73	1.39	Bradford *et al*. 1986
	Booroola-Rambouillet	USA	–	2.71	1.53	Schulze *et al*. 2003
	Booroola Merino	Australia	3.00	1.50	–	Davis 2005
	Romney sheep	New Zealand	6.24	4.05	2.03	Farquhar *et al*. 2006
	Deccani or Bannur	India	–	2.00	1.00	Nimbkar *et al*. 2008
	crossed with Garole		3.37	2.02	1.03	Pardeshi 2008
Litter size	Javanese thin tailed	Indonesia	–	2.31	1.38	Bradford *et al*. 1986
			2.59	1.95	1.24	Inounu *et al*. 1993
	Trangie Fertility × Dorset (TD) vs Booroola Dorset (BD)	Australia	–	2.07 (BD)	1.66 (TD)	Fogarty and Hall 1995
	Booroola-Rambouillet	USA	–	1.96	1.45	Schulze *et al*. 2003
	Garole Malpura (GM)	India	–	1.87	1.02	Sharma *et al*. 2004
	Booroola Merino	Australia	1.50	1.00	–	Davis 2005
	Chinese Merino	China	2.84	2.34	1.23	Guan *et al*. 2007
	Small tailed Han		1.40	1.11	–	Chu *et al*. 2007
	Awassi Breed	Israel	1.92	1.90	1.28	Gootwine *et al*. 2008
	Assaf Breed		2.55	2.40	1.68	
	Deccani or Bannur	India	–	1.60	1.00	Nimbkar *et al*. 2008
	crossed with Garole		2.01	1.83	1.01	Pardeshi 2008
	GM strain		2.17	1.73	1.03	Kumar *et al*. 2008b
			2.16	1.53	–	Anonymous 2012
	Kalehkoohi sheep	Iran	1.90	1.73	1.40	Mahdavi *et al*. 2014
Growth						
Birth weight (BW)	Assaf	Israel	4.03 kg	4.16 kg	4.32 kg	Gootwine *et al*. 2006
Mature body weight			67.30 kg	70.80 kg	70.10 kg	
BW	Chinese Merino	China	3.40 kg	3.40 kg	3.30 kg	Guan *et al*. 2007
3M weight			18.60 kg	18.00 kg	15.60 kg	
6M weight			23.50 kg	23.00 kg	22.60 kg	
BW	GM strain	India	3.50 kg	3.23 kg	2.61 kg	Kumar *et al*. 2008b
3 M weight			12.94 kg	14.05 kg	10.61 kg	
6 M weight			18.28 kg	22.56 kg	16.66 kg	
12 M weight			23.60 kg	29.14 kg	21.28 kg	
Wool	Trangie Fertility × Dorset (TD) vs Booroola Dorset (BD)	Australia	–	2.37 kg (BD)	2.66 kg (TD)	Fogarty *et al*. 1995
	Booroola-Rambouillet	USA	–	3.90	3.99	Schulze *et al*. 2003
	GMM vs Malpura	India	–	0.76 kg (GMM)	0.95 kg (Malpura)	Anonymous 2015
	Avishaan vs Patanwadi		–	0.95 kg (Avishaan)	1.35 kg (Patanwadi)	
Lamb survivability	Awassi	Israel	1.65	1.76	1.24	Gootwine *et al*. 2008
	Assaf		1.98	2.05	1.58	

castration (Price *et al.* 1991, 1992). It was speculated that high FSH concentration might influence higher sperm concentration in *FecB* carrier rams. Similarly, Booroola Merino ram had greater sperm output than Rambouillet and Columbia rams (Fitzgerald and Stellflug 1990). Texel rams carrying Booroola mutation had reported more libido than purebred Texel rams (Visscher *et al.* 2009).

Carcass traits: The effect of the *FecB* gene on mutton production traits was found to be negligible; however Booroola Merino crosses had enhanced carcass fatness (Kleemann *et al.* 1985, 1988). It was observed that Booroola Merino cross lambs had less intramuscular fat than the Bulgarian fine wool sheep (Dimitrov and Nedelchev 1999), however Booroola Merino cross lambs had more tender and larger eye muscle than Romney and Finnsheep crosses (Fahmy *et al.* 1992). Less intramuscular and high intermascular fat content was also shown in Booroola Merino cross lambs as compared to German Mutton merino lambs (Suess *et al.* 2000). Texel *FecB* carrier lambs had a higher dressing percentage and longissimus muscle depth and cross sectional area (Visscher *et al.* 2000). There were small differences found in the fatty acid composition between *FecB* carrier (Booroola Merino) and *FecB* non carrier (Suffolk and Pannon) sheep (Mezoszentgyorgyi *et al.* 2001). The study revealed that Booroola Merino sheep had significantly higher proportion of total quantity of saturated fatty acids and lower proportion of total quantity of unsaturated fatty acids as compared with *FecB* non-carrier sheep. The subcutaneous carcass fat was significantly higher in Booroola Leicestor (Booroola Merino × Border Leicester backcross) sired crossbred lambs than the first cross lambs (Fogarty *et al.* 2005). The overall study concluded that *FecB* gene might have little effect on carcass fat and muscle development in carrier lambs however it alters the fatty acid compositions.

Wool production: The fleece weight of the single copy *FecB* carrier ewes had been found to be lower than that of non-carrier ewes (Snowder and Shelton 1988), however many reports had revealed no significant difference between *FecB* carrier and *FecB* non-carrier Booroola Merino cross on wool production and wool quality traits (Ponzoni *et al.* 1985a, b; Fogarty *et al.* 1995, Walkden-Brown *et al.* 2007). *FecB* carrier sheep produced lower fleece weight as compared to *FecB* non-carrier sheep (Meyer *et al.* 1994, Southey *et al.* 2002). However, no significant differences were observed in greasy fleece yield (GFY) from *FecB* carrier and non-carrier Booroola-Rambouillet ewes (Schulze *et al.* 2003). It was theorized that the *Fec*B carrier animals are lighter than the non-carriers (Schulze *et al.* 2003, Kolte *et al.* 2005, Gootwine *et al.* 2006); and thus had relatively low surface area of carrier animals, resulting in low wool production. The 1st GFY was significantly lower in carriers (single and double copy) as compared to non-carriers in Garole × Malpura sheep (Mishra *et al.* 2008). Similarly, annual GFY was lower in *FecB* carrier patanwadi GMM crosses (Avishaan sheep) as compared to patanwadi sheep (Anonymous 2015).

Milk production: Introgression of the *FecB* gene increased the prolificacy of Awassi sheep, but the milk production of the F_1 Booroola-Awassi and its backcross progeny (BC_1) was reduced as compared with pure Awassi (Gootwine *et al.* 1993, Gootwine, 1995). It was hypothesized that the reduction in the milk might be due to the effect of other genes segregating through the Merinos (Gootwine *et al.* 1995). For improving the milk production, Awassi sheep was crossed with East Friesian sheep and later developed into Assaf breed (Gootwine and Goot 1996). In the subsequent study, it had been found that double copy *FecB* carrier (Afec-Awassi) ewes produced less milk than single copy *FecB* carrier ewes (Gootwine *et al.* 2006). In India, the average daily milk yield (ADMY) of Garole × Malpura ewes was significantly higher (P<0.05) in non-carrier as compared to carrier (Single and double copy) ewes. In contrast, the ADMY was significantly (P<0.01) higher in ewes those carry *FecB* gene with twin bearing lambs as compared to *FecB* carrier single bearing lambs and *FecB* non-carrier single bearing lambs (Mishra *et al.* 2008). Patanwadi inheritance further enhaced the ADMY in GMM × Patanwadi crosses (Prakash *et al*. 2019).

Lamb survivability: Survivability of twins and triplets is a concern in *FecB* introgression programs worldwide. The poor lamb survival had been reported in Booroola Merino as compared to control Merino ewes (Piper and Bindon 1987, Davis *et al.* 1991). The lamb survival rate in Booroola Merino crosses was 9.8% lower than that of local breed (Davies *et al.* 1991). *FecB* carrier Booroola-Rambouillet backcross ewes had lambs with lower survival rates as compared to non-carrier ewes (Notter *et al.* 2009). The lamb survival rate in non-carrier Awassi and Assaf sheep at birth was reported as 0.98 and 0.94, respectively (Gootwine *et al.* 2008). The lamb survival rate was declined to 0.93 and 0.86 in single and double copy of *FecB* carrier Awassi sheep; and 0.85 and 0.78 in single and double copy of *FecB* carrier Assaf ewes, respectively (Gootwine *et al.* 2008). It had been hypothesized that homozygous Booroola ewes had a combination of inferior fertility, lower lamb survival rate and weaned less lambs than the heterozygous Booroola ewes (Walkden-Brown *et al.* 2009). Study conducted on triple breed cross Avishaan sheep with *FecB* gene revealed the survivability figures during pre- and post weaning of lambs and adult stage were 92.60, 99.10 and 98.80%, respectively with overall survivability of 97.70% (Sharma *et al.* 2020).

Fixing the prolificacy in sheep reared in extensive or semi intensive management system

The results of the experiments conducted worldwide on *FecB* introgression programs suggest that high prolificacy is economically beneficial under intensive and semi-intensive management system of sheep rearing. However, it is often an undesirable trait under extensive system because the overall productivity of prolific sheep may reduce due to the high mortality rate of the lambs, low birth weight of individual lamb, insufficient milk yield of the ewe to sustain the mutltiple lambs, unaccustomed managemental obligation, etc. The effects of the *FecB* gene on reproductive traits viz. ovulation rate and liiter size are described in the literature with similar results (Montgomery *et al.* 1992, Smith *et al.* 1993, 1996; Campbell *et al.* 2003, Kumar *et al.* 2008b, Sharma *et al.* 2020); however, the effects of the *FecB* gene on production traits have varied opinions. Lambs from multiple births have low birth weight leading to poor survivability, especially under extensive system (Owens *et al.* 1985). The Booroola Merino × Dorset *FecB* carrier ewes was reported to be heavier than the non-carrier ewes (Fogarty *et al.* 1995). Several studies had observed that there was no difference in birth weight and growth rates between *FecB* carrier ($FecB^{BB}$ and $FecB^{B+}$) and non-carrier ($FecB^{++}$) lambs (Visscher *et al.* 2000, Southey *et al.* 2002, Abella *et al.* 2005, Walkden-Brown *et al.* 2007); however others had found that *FecB* carrier lambs had a relatively lower birth weight and growth rate as compared to non-carrier lambs (Davis *et al.* 1991, Montgomery *et al.* 1991, Gootwine *et al.* 1993, Nowak and Charon 2001, Schulze *et al.* 2003, Kolte *et al.* 2005). It was hypothesized that Booroola gene might be closely linked to a QTL affecting growth rate from birth to weaning (Walling *et al.* 2000). In another study, it was theorized that the genotype of lamb had no effect on birth weight or post weaning average daily gain (ADG), but the difference might be due to type of birth and sire effects (Willingham *et al.* 2002). Similarly, it was reported that the birth weight and post weaning growth rate of the $FecB^{BB}$ lambs were lower than that of $FecB^{B+}$ and $FecB^{++}$ Booroola-Assaf lambs (Gootwine *et al.* 2006). Heavy birth weight can be achieved by using larger size recipient ewes (Naqvi *et al.* 2006). Lower body weight and average daily gain starting from birth to 12 month of age were also reported in Garole × Malpura halfbred lambs as compared to Malpura lambs (Sharma *et al.* 2004, Kumar et al 2008b). In contrast, a positive effect of *FecB* on early postnatal body weight was found in Chinese Merino prolific meat strain (Guan *et al.* 2007).

FecB *introgression*

Global experience: The *FecB* gene mutation has probably been present in Australia since 1792 or 1793 when the first shipments of the highly fecund 'Bengal sheep' from Calcutta, India had arrived (Turner 1982). The*FecB* introgression into Awassi and Assaf sheep in Israel was started in 1986 (Gootwine 2008) and the improved genotypes have been most successful to date in fully intensive dairy and non-dairy production systems with intensive rearing of lambs. As in the Australian experience, the heterozygote is more productive than the homozygote carrier due to higher lamb survival despite similar litter size (LS). Typical LS of the Awassi are 1.31, 1.90 and 1.92 for 0, 1 and 2 copies of *FecB,* respectively and the equivalent values for the Assaf was 1.68, 2.40 and 2.55, respectively. In USA, introgressions of *FecB* into Rambouillet genetic background occurred in the mid-1980s. Many studies conducted in USA showed little opportunity for use of *FecB* in commercial sheep production pimarily due to high prolificacy levels was already present in several US sheep breeds and secondly the desire by most US producers to avoid high frequencies of triplet births in order to avoid high lamb mortality. Under Indonesian conditions where nutrition is good, ewes carrying one copy of *FecB* exhibit the highest gross margin, followed by homozygotes then non-carriers. Under conditions of poor nutrition there was no economic benefit of *FecB* at all. Typical LS of the Indonesian Thin Tailed sheep are 1.22, 2.02 and 2.5 for 0, 1 and 2 copies of *FecB*, respectively, with respective lamb survival to 90 days being 84.3%, 71.9% and 59.2% (Inounu and Priyanti 2008). *FecB* introgression into French Mérinos dArles sheep in France was commenced in 1983. Teyssier *et al.* (2008) reported on datasets collected from both an institutional farm and a commercial producer. There was a clear economic advantage for *FecB* heterozygote ewes based on consistent production of 50-65% additional lambs for sale or replacement. A further study of prolific sheep had revealed that *FecB* was also present in two Chinese sheep breeds (Davis *et al.* 2006). All of the Hu sheep sampled were homozygous carriers of *FecB*, whereas all three *FecB* genotypes were present in the Small Tail Han sheep. Lately *FecB* gene had also been detected in Iranian Kalehkoohi sheep (Mahdavi *et al.* 2014).

Indian experience: Sheep husbandry is backbone of rural economy in India. It is important as it helps to sustain the livelihood of rural poor in difficult terrains characterized by sparse vegetation, marginal land and a high incidence of poverty. India is endowed with wide diversity of sheep genetic resources. Sheep husbandry faces a dilemma to produce more animal protein for the growing human population against the reality of shrinking grazing resources, creating a major constraint to the further growth of sheep population. Demand for meat in India has increased rapidly and the emphasis has shifted from wool towards mutton as the main produce. There is acute shortage of meat for domestic need besides huge demand in the international market. The gap between the demand and production of mutton could be bridged by augmenting the reproductive rate by introducing prolificacy. Improving prolificacy in sheep flock can increase the profitability of sheep production. In order to improve the fecundity of sheep, introgression of *FecB* mutation from prolific sheep into the non-carrier non-prolific sheep is an ideal approach to evolve a large size breed capable of multiple births for economic and remunerative mutton production.

NARI, Phaltan experience: The Nimbkar Agricultural Research Institute (NARI), Phaltan, Maharashtra introduced the *FecB* mutation into the Deccani breed from the Garole sheep to increase lamb production and income of smallholder shepherds. Artificial insemination was used because the small size of Garole rams precluded natural mating. Two fecund strains were developed-the NARI Suwarna, with contributions from only Garole and Deccani breeds, and the NARI Composite, with additional contributions from Awassi and/or Bannur breeds (Nimbkar *et al.* 2008). Study revealed that one copy of *FecB* led to an increase in live litter size (LS) at birth from 1.0 to 1.6 in the NARI flock and from 1.0 to 1.4 in smallholder flocks. Less than 5% of the litters of single copy *FecB* carrier ewes were triplets. Thus, the introduction of the *FecB* mutation in Deccani sheep had proved to be successful in increasing both lamb production and incomes. NARI had also begun to disseminate *FecB*-carrier rams and ewes and surveyed 23 participating sheep owners. In general, the sheep owners' responses to twin lambs were positive. Twin lambs were viewed as more profitable than single lambs, with the main disadvantage cited as the need to undertake supplementary feeding and management to ensure adequate growth rates and survival of twin lambs (Prior *et al.* 2008).

ICAR-CSWRI, Avikanagar experience: Information on prolificacy in sheep were available in public domain around late 1980s, however ICAR-Central Sheep and Wool

Research Institute (CSWRI) initiated cross breeding scheme during 1997 to explore the possibility of incorporating fecundity gene from India's most valuable germplasm 'Garole sheep' of West Bengal into the non-prolific and large size mutton sheep breed 'Malpura' of Rajasthan (Sharma *et al.* 2004) and produced the Garole × Malpura (GM) crossbred carrying the *FecB* mutation. Encouraging results were obtained in Garole × Malpura (GM) half-breds in terms of twin lambing percentage to the tune of 45.70% as compared to Malpura with 2.50%. The litter size at birth and weaning in GM halfbred were reported to be 1.46 and 1.19 and in Malpura there were 1.02 and 0.97, respectively Sharma *et al.* (2004). A single mutated copy of *FecB* gene produced 0.70 and weaned 0.58 extra lambs in GM sheep (Mishra *et al.* 2009). Having developed prolific Garole × Malpura (GM) half-bred sheep, there was scope to exploit the prolific GM sheep for relatively better growth by backcrossing with native Malpura. In the backcrossing programme, the *FecB* gene carrier GM rams were used as sires and Malpura ewes as dam breed to produce the GM × Malpura (GM (M); 75% Malpura and 25% Garole) and reciprocal crosses were also attempted to produce M (GM). The 3/4th crossbreds GMM ewes were capable of producing more than 60% multiple lambings and also have higher body weight compared to half-breds but problem of low milk yield in dam persisted and body weights of GMM lambs also needed to be improved further. To overcome the problem of low milk yield in the 3/4th crossbreds dams and to enhance the live weights of lambs, Patanwadi inheritance (a heavy sheep breed of Saurashtra region of Gujarat and famous for milk yield) was introduced during 2008. The GMM having double copy *FecB* carrier gene was used as sire and Patanwadi was used as a dam breed to produce triple indigenous breed crosses (Garole-Malpura-Patanwadi). With the implementation of structured breeding plan and *FecB* gene detection, a high performing sheep strain 'Avishaan' in terms of high prolificacy, more litter weight, more milk per dam and adaptable to harsh climatic conditions was developed by CSWRI and released on 4th January 2016 (Sharma *et al.* 2017). This developed prolific Avishaan strain is a composite cross possessing 12.5% Garole, 37.5% Malpura and 50% Patanwadi inheritance in which *Fec*B mutation has been introgressed. With goal oriented research efforts, the prolificacy in Avishaan sheep has increased as high as 74.4% with litter size of 1.80 (Sharma *et al.* 2020). The average live weights at birth, three, six and twelve months of age of the Avishaan lambs were 2.60, 15.00, 23.50 and 29.70 kg, respectively (Sharma *et al.* 2020).

Malpura versus its crosses with prolific Garole: The data for ewe productivity efficiency (EPE) over a period of five years (2011-2015) were analyzed for Avishaan, GMM and native Malpura sheep (Sharma *et al.* 2017). EPE is a production efficiency trait computed as described elsewhere (Sharma *et al.* 2004). The newly developed Avishaan sheep excelled the monotoccus Malpura sheep in EPE at 3 months of lambs by 33.00% by harvesting 20.65 kg at weaning whereas Malpura sheep harvested only 15.58 kg at weaning of lamb. Also the EPE of Avishaan was found to be higher by 35% as compared to EPE of prolific GMM crosses.

Way forward in enhancing sheep prolificacy

Booroola fecundity gene introgression programmes have reached mature stage in many countries including India. Newer technologies can be applied to further enhance the sheep prolificacy. The mutated BMPR1B protein may be produced *in vitro* or its antibody particularly for extra cellular domain (BMPR-1B) which may block the BMPR-1B receptor and there would not be enough space for binding the ligand molecules (like BMP-2, BMP-4 and GDF-5) that may impair the signalling cascades and leads to more folliculogenesis (like in Booroola mutation). Thus, administration of the antibody against the BMPR-1B in sheep may be used as 'fecundity vaccine' for improving the ovulation rate in non-prolific sheep. Assisted reproduction technologies can also be used to further enhance the prolificacy in monotoccus ewes. Prolific ewes and non prolific counterparts can be selected, synchronized by progesterone sponges and superovulated using optimal doses of FSH. The ovulation rate of superovulated females may be checked through laparoscopy and performed natural mating with Avishaan rams possessing double copy of *FecB* gene. After 4-5 days of mating, the embryos can be collected and transferred into synchronized recipient ewes using laparoscopy. Pregnancy can be confirmed by the ultrasonography. In cotarary, prolific ewes can be synchronized and superovulated. After slaughter, ewe's ovaries can be retrieved and the follicles can be matured *in vitro*. The matured oocytes can be *in vitro* fertilized by diluted double copy *FecB* carrier Avishaan semen. The cleaved embryos may be cultured upto blastocyst stage. The blastocysts can be transferred into synchronized recipients to develop the cloned prolific sheep. The transgenic animals for higher fecundity (mutated BMPR-1B) can be produced, if this mutated receptor could be transferred directly into an embryo or by using the embryonic stem cells of *FecB* carrier animals for production of highly prolific cloned sheep in the near future. Genome editing technologies can also be applied to sheep embryos for editing the sheep BMPR1B gene (Zhou *et al.* 2018; 2020).

Conclusion

Production performance of animal is governed by both genetic and environmental factors. The utilization of prolificacy as an economically important trait is continuing since many decades. After confirmation of *Fec*B gene responsible for the prolificacy in sheep, introgression of this mutation in many non-carrier monotocus sheep were introduced worldwide. Advent of molecular techniques to analyze precisely *FecB* carrier status catalyzed the *FecB* introgression efforts to enhance sheep prolificacy. Being a major gene and having direct correlation with high fecundity, it became one of the widely studied genes in the world. Most of the developed countries showed initial enthusiasm and expectation of practical application through introgression of *FecB* gene in local breeds. But later on due to high frequencies of triplet births, which required more intensive management for economic gain made the pace of *FecB* introgression programme slow. Israel experience had shown economic benefits of introgression of *FecB* gene in Awassi and Assaf breeds of sheep and NARI reported successful introgression of *FecB* into non-fecund Deccani sheep in India. This has not resulted in the unmanageable litter size experienced in other countries and is associated with positive effects on biological and economic efficiency. Similarly, CSWRI reported quite enthusiastic results with the crossing of Malpura with Garole and initial results with respect to production status and survivability improvement in triple breed cross (Garole, Malpura and Patanwadi) has paved a new way to further enhance the lamb production and high litter survival up to market age. We foresee application of this terminal technology in the farmer's flock where it shall probably lead to socio-economic upliftment of farmers. The Booroola fecundity is very economical for improving the prolificacy of non-prolific sheep breeds. But care has to be taken before implementation of the *Fec*B introgression programme in sheep flock. Sufficient nutrition and post natal care are required to be provided to the lambs and mother particularly up to weaning stage to reduce the mortality of the lambs born as twins or triplets. There are several challenges for using *Fec*B gene in the future using assisted reproductive, genome editing and transgenic technology. *FecB* is generally associated with reduced birth weight and susquent growth rate but remains economically viable for intensive and semi-intensive system of rearing.

REFERENCES

Abella D F, Cognie Y, Thimonier J, Seck M and Blank M R. 2005. Effects of the *FecB* gene on birth weight, postnatal growth rate and puberty in Booroola × Mérinos d'Arles ewe lambs. *Animal Research* **54**: 283–88.

Anonymous. 2012. Annual Report. ICAR-Central Sheep and Wool Research Institute, Avikanagar, Rajasthan, India pp. 51.

Anonymous. 2015. Annual Report. ICAR–Central Sheep and Wool Research Institute, Avikanagar, Rajasthan, India. pp. 58.

Bradford G E, Quirke J F, Sitorus P, Inounu I, Tiesnamurti B, Bell F L, Fletcher I C and Torell D T. 1986. Reproduction in Javanese sheep: Evidence for a gene with large effect on ovulation rate and litter size. *Journal of Animal Science* **63**(2): 418–31.

Campbell B K, Baird D T and Souza C J H. 2003. The *FecB* (Booroola) gene acts at the ovary: *in vivo* evidence. *Reproduction* **126**: 101–11.

Chong Y Q, Liu G Q and Jiang X P. 2019. Effect of BMPRIB gene on litter size of sheep in China: A meta-analysis. *Animal Reproduction Science* **210**: 106–75.

Chu M X, Liu Z H, Jiao C L, He Y Q, Fang L, Ye S C, Chen G H and Wang J Y. 2007. Mutations in BMPR-1B and BMP-15 genes are associated with litter size in small tailed Han sheep (*Ovis aries*). *Journal of Animal Science* **85**(3): 598–603.

Davis G H, Balakrishnan L, Ross I K, Wilson T, Galloway S M, Lumsden B M, Hanrahan J P, Mullen M, Mao X Z, Wang G L, Zhao Z S, Zeng Y Q, Robinson J J, Mavrogenis A P, Papachristoforou C, Peter C, Baumung R, Cardyn P, Boujenane I, Cockett N E, Eythorsdottir E, Arranj J J, and Notter D R. 2006. Investigation of the Booroola (*FecB*) and Inverdale (*FecX^I*) mutations in 21 prolific breeds and strains of sheep sampled in 13 countries. *Animal Reproduction Science* **92**: 87–96.

Davis G H, Elsen J M, Bodin L, Fahmy M, Gootwine E, Bor A, Braw-Tal R, Lengyel A and Paszthy G. 1991. A comparison of the production from Booroola and local breed sheep in different countries. *Proceeding of the 2nd International Workshop on Major Genes for Reproduction in Sheep*. (Eds) J. M. Elsen, L. Bodin and J. Thimonier. pp. 315–23. INRA, Paris, France.

Davis G H, Galloway S M, Ross I K, Gregan S M, Ward J, Nimbkar B V, Ghalsasi P M, Nimbkar C, Gray G D, SubandriyoInounu I, Tiesnamurti B, Martyniuk E, Eythorsdottir E, Mulsant P, Lecerf F, Hanrahan J P, Bradford G E and Wilson T. 2002. DNA tests in prolific sheep from eight countries provide new evidence on origin of the Booroola (*FecB*) mutation. *Biology of Reproduction* **66**: 1869–74.

Davis G H, Montgomery G W, Allison A J, Kelly R W and Bray A R. 1982. Segregation of a major gene influencing fecundity in progeny of Booroola sheep. *New Zealand Journal of Agricultural Research* **25**: 525–29.

Davis G H. 2004. Fecundity genes in sheep. *Animal Reproduction Science* **82/83**: 247–53.

Davis G H. 2005. Major genes affecting ovulation rate in sheep. *Genetic, Selection and Evolution* **37(1)**: s11–s23.

Dimitrov D and Nedelchev D. 1999. Study on growth intensity and meat quantity of lambs crosses between Booroola and north-east Bulgarian finewool sheep. *Zhivotnovdni Nauki* **36**: 11–15.

Epstein H. 1985. The Awassi sheep with special reference to the improved dairy type. *Animal Production and Health* paper No. **57**, FAO, Rome.

Fahmy M H, Boucher J M, Poste L M, Gregoire R, Butler G and Comeau J E. 1992. Feed efficiency, carcass characteristics, and sensory quality of lambs, with or without prolific ancestry, fed diets with different protein supplements. *Journal of Animal Science* **70**: 1365–74.

Farquhar P A, Dodds K G and Davis G H. 2006. Introgression of the Booroola mutation (*FecB*) leads to hyper-prolificacy in a Romney sheep flock. *Proceedings of 8th World Congress on Genetics Applied to Livestock Production*. Belo Horizonte, Minas Gerais, Brazil, 13–18 August, pp 04–33.

Fitzgerald J A and Stellflug J N. 1990. Comparison of scrotal circumferences, sperm output and libodo of Booroola Merino, Polypay, Rambouillet and Columbia rams in a controlled photoperiod. *Sheep Research Journal* **6**: 11–14.

Fogarty N M and Hall D G. 1995. Performance of crossbred progeny of Trangie Fertility Merino and Booroola Merino rams and Poll Dorset ewes. 3. Reproduction, live weight, and wool production of adult ewes. *Australian Journal of Experimental Agriculture* **35**: 1083–91.

Fogarty N M, Hall D G and Atkinson W R. 1992. Productivity of three crossbred ewe types mated naturally at 8-monthly intervals over two years. *Australian Journal of Agricultural Research* **43**: 1819–32.

Fogarty N M, Hall D G and Gilmour A R. 1995. Performance of crossbred progeny of Trangie Fertility Merino and Booroola Merino rams and Poll Dorset ewes. 2: Reproductive activity, liveweight and wool production of ewe lambs. *Australian Journal of Experimental Agriculture* **35(8)**: 1075–82.

Fogarty N M, Ingham V M, Gilmour A R, Cummins L J, Gaunt G M, Stafford J, Hocking Edwards J E and Bank R G. 2005. Genetic evaluation of crossbred lamb production. 2. Breed and fixed effects for post weaning growth, carcass, and wool of first-cross lambs. *Australian Journal of Agricultural Research* **56**: 455–63.

Gootwine E and Goot H. 1996. Lamb and milk production of Awassi and East Friesian sheep and their crosses under Mediterranean environment. *Small Ruminant Research* **20**: 255–60.

Gootwine E, Bor A, Braw-Tal R and Zenou A. 1995. Reproductive performance and milk production of the improved Awassi breed as compared to its crosses with the Booroola Merino. *Animal Science* **60**: 109–15.

Gootwine E, Bor A, Braw-Tal R and Zenu A. 1993. Inheritance of birth weight and growth traits in crosses between the Booroola-Merino and Assaf sheep breeds. *Livestock Production Science* **33**: 119–26.

Gootwine E, Reicher S and Rozov A. 2008. Prolificacy and lamb survival at birth in Awassi and Assaf sheep carrying the *FecB* (Booroola) mutation. *Animal Reproduction Science* **108** (3-4): 402–12.

Gootwine E, Rozov A, Bor A and Reicher S. 2003. Effects of the *FecB* (Booroola) gene on reproductive and productive traits in the Assaf breed. '*Proceedings of the International Workshop on Major Genes and QTL in Sheep and Goats*'. CD-ROM com. no. 2-12, p. 4. Toulouse, France.

Gootwine E, Rozov A, Bor A and Reicher S. 2006. Carrying the (Booroola) mutation is associated with lower birth weight and slower post-weaning growth rate for lambs as well as a lighter mature body weight for ewes. *Reproduction, Fertility and Development* **18**: 433–37.

Gootwine E. 1995. Increasing prolificacy of the fat tail Awassi sheep using the Booroola *FecB* gene. *Cahiers Options Mediterraneennes* **11**: 79–87.

Gootwine E. 2008. Biological and economic consequences of introgressing the B allele of the *FecB* (Booroola gene) into Awassi and Assaf sheep. Pp. 107–117. 'Using the *FecB* (Booroola) gene in sheep breeding programs'. *Proceedings of International Booroola Workshop held in NARI, Phaltan*, 10-12 November 2008. (Eds) S. W. Brown, C. Nimbkar, J.V. Werf and V. Gupta. NARI, Maharashtra, India.

Guan F, Liu S R, Shi G Q and Yang L G. 2007. Polymorphism of *FecB* gene in nine sheep breeds or strain and its effect on litter size, lamb growth and development. *Animal Reproduction Science* **99**: 44–52.

Hanrahan J P. 1980. Ovulation rate as the selection criterion for litter size in sheep. *Proceedings of the Australian Society of Animal Production* **13**: 405–08.

Inounu I and Priyanti A. 2008. Biological and economic consequences of the *FecB* mutation in Indonesian thin tailed sheep. Pp. 126-132. 'Using the FecB (Booroola) gene in sheep breeding programs'. *Proceedings of International Booroola Workshop held in NARI*, Phaltan, 10-12 November 2008. (Eds) S. W. Brown, C. Nimbkar, J.V. Werf and V. Gupta. NARI, Maharashtra, India.

Inounu I, Iniguez L, Bradford G E, Subandriyo and Tiesnamurti B. 1993. Production performance of prolific Javanese ewes. *Small Ruminant Research* **12**(3): 243–57.

Kleemann D O, Ponzoni R W, Stafford J E and Grimson R J. 1985. Growth and carcass characters of South Australian Merino and its crosses with the Booroola and Trangie Fertility Merino. *Australian Journal of Experimental Agriculture* **25**: 750–57.

Kleemann D O, Ponzoni R W, Stafford J E and Grimson R J. 1988. Carcass composition of the South Australian Merino and its crosses with the Booroola and Trangie Fertility Merino. *Australian Journal of Experimental Agriculture* **28**: 167–71.

Kleemann D O, Walker S K, Walkley J R W, Smith D H, Grimson R J and Seamark R F. 1990. Fertilization and embryo loss in Booroola Merino × South Australian Merino ewes: effect of the F gene. *Theriogenology* **33**: 487–98.

Kolte A P, Mishra A K, Kumar S, Arora A L and Singh V K. 2005. A study on effect of carrying *FecB* gene on body weight in Garole and Malpura sheep. *Asian Australasian Journal of Animal Sciences* **18**: 1379–82.

Kumar D, Joshi A, Naqvi S M K, Kumar S, Mishra A K, Maurya V P, Arora A L, Mittal J P and Singh V K. 2007. Sperm motion characteristics of Garole × Malpura sheep evolved in a semi-arid tropical environment through introgression of *FecB* gene. *Animal Reproduction Science* **100**: 51–60.

Kumar S, Kolte A P, Mishra A K, Arora A L and Singh V K. 2006. Identification of *FecB* mutation in Garole × Malpura sheep and its effect on litter size. *Small Ruminant Research* **64**: 305–10.

Kumar S, Mishra A K, Kolte A P, Arora A L, Singh D and Singh V K. 2008b. Effect of the Booroola (*Fec B*) genotypes on growth performance, ewe's productivity efficiency and litter size in Garole × Malpura sheep. *Animal Reproduction Science* ***105***: 319–31.

Kumar S, Mishra A K, Kolte A P, Dash S K and Karim S A. 2008a. Screening for Booroola (*FecB*) and Galway ($FecX^G$) mutations in Indian sheep. *Small Ruminant Research* **80**: 57–61.

Mahdavi M, Nanekarani S and Hosseini S D. 2014. Mutation in BMPR-IB gene is associated with litter size in Iranian Kalehkoohi sheep. *Animal Reproduction Science* **147**: 93–98.

Meyer H H, Bigham M L, Baker R L, Harvey T G and Hickey S M. 1994. Effects of Booroola Merino breeding and the *FecB* gene on performance of crosses with longwool breeds. 1. Effects on growth, onset of puberty, wool production and wool traits. *Livestock Production Science* **39**: 183–90.

Mezoszentgyorgyi D, Husveth F, Lengyel A, Szegleti C and Komlosi I. 2001. Genotype-related variations in subcutaneous fat composition in sheep. *Animal Science* **72**: 607–12.

Mishra A K, Arora A L, Kumar S and Prince L L L. 2009. Studies on effect of Booroola (*FecB*) genotype on life time ewe's productivity efficiency, litter size, and number of weaned lambs in Garole × Malpura sheep. *Animal Reproduction Science* **113**: 293–98.

Mishra A K, Kumar S, Kolte A P, Arora A L and Singh V K. 2008. Effect of the *FecB* gene on greasy fleece yield and milk yield of Garole x Malpura sheep. *Indian Journal of Animal Sciences* **78** (9): 971–74.

Montgomery G W, Crawford A M, Penty G M, Dodds K G, Ede A J, Hennery H M, Pierson C A, Lord E A, Galloway S M, Schmack A E, Sise J A, Swabrick PA, Hanrahan V, Buchanan F C and Hill D F. 1993. The ovine Booroola fecundity gene (*FecB*) is linked to markers from a region of human chromosome 4q. *Nature Genetics* **4**: 410–14.

Montgomery G W, Lord E A, Penty G M, Dodds K G, Board T E, Cambridge L M, Suden S L F, Stone R T and Crawford A M. 1994. The Booroola fecundity (*FecB*) gene maps to sheep chromosome 6. *Genomics* **22**: 148–53.

Montgomery G W, McNatty K P and Davis G H. 1992. Physiology and molecular genetics of mutations that increase ovulation rate in sheep. *Endocrine Reviews* **13**: 309–28.

Mulsant P, Lecerf F, Fabre S, Schibler L, Monget P, Lanneluc I, Pisselet C, Riquet J, Monniaux D, Callebaut I, Cribiu E, Thimonier J, Teyssier J, Bodin L, Cognie Y, Chitour N and Elsen J M. 2001. Mutation in the bone morphogenetic protein receptor-IB is associated with increased ovulation rate in Booroola ewes. *Proceedings of the National Academy of Sciences USA* **98**: 5104–09.

Naqvi S M K, Joshi A, Gulyani R, Kumar D, Kolte A P, Kumar S, Maurya V P, Saha S, Mittal J P and Singh V K. 2006. Production of prolific microsheep from large size non-prolific sheep through embryo transfer. *Veterinary Record* **159**: 522–26.

Nimbkar C, Ghalsasi P M, Nimbkar B V, Ghalsasi P P, Gupta V S, Pardeshi V C, Maddox J F, van der Werf J H J, Gray G D and Brown S W. 2008. Biological and economic consequences of introgression of the *FecB* (Booroola) gene into Deccani sheep. Pp. 75-87. 'Using the FecB (Booroola) gene in sheep breeding programs'. *Proceedings of International Booroola Workshop held in NARI*, Phaltan, 10-12 November 2008. (Eds) S. W. Brown, C. Nimbkar, J.V. Werf and V. Gupta. NARI, Maharashtra, India.

Nimbkar C, Ghalsasi P M, Swan A, Walkkden-Brown S W, Kahn L P. 2003. Evaluation of growth rates and worm resistance of Deccani and Bannur lambs and their crosses with Garole. *Animal Science* **76**: 503–15.

Notter D R, Thomas D L and Waldron D F. 2009. Biological and economic consequences of the *FecB* mutation in the USA. *Proceedings of the Helen Newton Turner Memorial International Workshop on using the FecB (Booroola) gene in sheep*. ACIAR Proceedings Series.

Nowak Z and Charon K M. 2001. Identification of fecundity gene (*FecB*) carriers using microsatellite markers and its effect on sheep weight. *Journal of Applied Genetics* **42**: 49–57.

Owens J L, Bindon B M, Edey T N and Piper L R. 1985. Behaviour at parturition and lamb survival of Booroola Merino sheep. *Livestock Production Science* **13**: 359–72.

Pardeshi V C. 2008. '*A study towards genetic diversity and genetic basis of prolificacy in important sheep breeds of India*'. Ph.D. Thesis submitted to University of Mumbai. pp. 93.

Piper L R and Bindon B M. 1982. The Booroola Merino and the performance of medium non-Peppin crosses at Armidale. 'The Booroola Merino'. (Eds) L. R. Piper, B. M. Bindon and R. D. Nethery., pp. 9–19. CSIRO: Armidale, Australia.

Piper L R and Bindon B M. 1987. Industry utilization of the Booroola Merino in Australia. 'Merino improvement programs in Australia'. (Ed.) B. McGuirk. pp. 279–82. Australian Wool Corporation: Melbourne, Australia.

Piper L R and Bindon B M. 1996. The Booroola Merino. 'Prolific Sheep'. (Ed.) M. H. Fahmy. pp. 152–160. CAB International, Willingford, UK.

Piper L R, Bindon B M and Davis G H. 1985. The single gene inheritance of the high litter size of the Booroola Merino. Pp 115–25. 'Genetics of Reproduction in Sheep'. (Eds) R.B. Land and D.W. Robinson. Butterworths London, UK. pp.115–25.

Ponzoni R W, Fleet M R, Walkley J R W and Walker S K. 1985a. A note on the effect of the F gene on wool production and live weight of Booroola × South Australian Merino rams. *Animal Production* **40**: 367–69.

Ponzoni R W, Walker S K, Walkley J R W and Fleet M R. 1985b. The productivity of Bungaree, Booroola × Bungaree and Trangie Fertility × Bungaree Merino ewes in South Australia. '*Genetics of Reproduction in Sheep*'. (Eds) by R. B. Land and D. W. Robinson. Butterworths, London, UK. Pp. 127–137.

Prakash Ved, Sharma R C, Prince L L L and Kumar A. 2019. Milk yield potential of prolific Avishaan and GMM sheep and their association with overall ewe productivity. *Indian Journal of Small Ruminants* **25**(1): 25–30.

Price C A, Hudson N L and McNatty K P. 1991. Effects of castration on plasma LH and FSH concentrations in adult rams which were homozygous carriers or non-carriers of the Booroola fecundity gene. *Journal of Reproduction and Fertility* **93**: 211–19.

Price C A, Hudson N L and McNatty K P. 1992. Effect of testosterone and bovine follicular fluid on concentrations of luteinizing hormone and follicle stimulating hormone in plasma of castrated rams that are homozygous carriers or non-carriers of the Booroola fecundity gene. *Journal of Reproduction and Fertility* **95**: 947–57.

Prior J, Ghalsasi P M, Brown S W, Chavan K M, Kulkarni S R and Nimbkar C. 2008. Shepherd's views on the value and management of Deccani crossbred *FecB* carrier ewes with a higher twinning percentage: implications for a future introgression extension program. Pp. 175–91. 'Using the FecB (Booroola) gene in sheep breeding programs: proceedings of International Booroola Workshop held in NARI, Phaltan, 10-12 November 2008', ed. by S. W. Brown, C. Nimbkar, J.V. Werf and V. Gupta. NARI, Maharashtra, India.

Schulze K S, Waldron D F, Willingham T D, Shelby D R, Engdahl G R, Gootwine E, Yoshefi S, Montgomery G W, Tate M L and Lord E A. 2003. Effects of the *FecB* gene in half-sib families of Rambouillet-cross ewes. *Sheep and Goat Research Journal* **18**: 83–88.

Sharma R C, Aroral A L, Mishra A K, Kumar S and Singh V K. 2004. Breeding prolific Garole with Malpura sheep for increased reproductive efficiency in semi arid tropics of India. *Asian Autralasian Journal of Animal Sciences* **17** (6): 737–42.

Sharma R C, Gowane G R, Kumar A, Kumar R and Mallick P K. 2020. Studies of prolificacy aspect in triple breed cross Avishaan sheep in semi-arid region of Rajasthan. *Proceedings of National Symposium on Physiological Approaches to Address Environment Challenges for Increasing Animal Productivity and Farmer's Income* (SAPICON-2020) held at ICAR-CSWRI, Avikanagar, Rajasthan during February 18–19, 2020. pp 178.

Sharma R C, Prince L L L, Prakash V, Gowane G R, Kumar A Kumar S and Naqvi S M K. 2017. Productivity efficiency of Avishaan ewes under semi arid conditions of Rajasthan. Proceedings of *National Seminar on Improvement of Small Ruminant Production System for Livelihood Security* held at ICAR–CSWRI, Avikanagar during March 9–10, 2017. pp 82.

Shimasaki S, Moore R K, Otsuka F and Erickson G F. 2004. The bone morphogenetic protein system in mammalian reproduction. *Endocrine Reviews* **25**: 72–101.

Singh R V, Sivakumar A, Sivashankar S, Das G, Walkden-Brown SW, Werf J H J V D, Nimbkar C, and Gupta V S. 2009. Evaluation of the Booroola (*FecB*) gene in Muzaffarnagari sheep. *ACIAR Proceedings. Series* **133**: 223–24.

Smith P, Hudson N L, Corrigan K A, Shaw L, Smith T, Phillips D J and McNatty K P. 1996. Effects of the Booroola gene (*FecB*) on body mass, testis development and hormone concentrations during fetal life. *Journal of Reproduction and Fertility* **108**: 253–61.

Smith P, O WS, Hudson N L, Shaw L, Heath D A, Condell L, Phillips D J and McNatty K P. 1993. Effects of the Booroola gene (*FecB*) on body weight, ovarian development and hormone concentrations during fetal life. *Journal of Reproduction and Fertility* **98**: 41–54.

Snowder G D and Shelton M. 1988. The relationship of lamb and wool production in range Rambouillet ewes. *SID Research Journal* **4**: 1–5.

Southey B R, Thomas D L, Gottfredson R G and Zelinsky R D. 2002. Ewe productivity of Booroola Merino-Rambouillet crossbred sheep during early stages of the introgression of the *FecB* allele into a Rambouillet population. *Livestock Production Science* **75**: 33–44.

Souza C J H, MacDougall C, Campbell B K, McNeilly A S and Baird D T. 2001. The Booroola (*FecB*) is associated with a mutation in the bone morphogenetic protein receptor type 1b (BMPR1B) gene. *Journal of Endocrinology* **169**: R1–R6.

Suess R, Heylen K and von Lengerken G. 2000. The effect of Booroola- Merino on the fat content and fat quality of carcasses in crosses with German Mutton Merinos. *Archiv Fuer Tierzucht* **43**: 45–56.

Teyssier J, Bodin L, Maton C, Bouquet P M and Elsen J M. 2008. Biological and economic consequences of the *FecB* gene into the French Merinos d'Arles sheep. Pp. 143–149. Using the *FecB* (Booroola) gene in sheep breeding programs. Proceedings of International Booroola Workshop held in NARI, Phaltan, 10-12 November 2008. (Eds) S. W. Brown, C. Nimbkar, J.V. Werf and V. Gupta. NARI, Maharashtra, India.

Teyssier J, Elsen J M, Bodin L, Bosc P, Lefevre C and Thimonier J. 1998. Three-year comparison of productivity of Booroola carriers and non-carrier Merino d'Arles the *FecB* gene in half-sib families of Rambouillet-cross ewes. *Sheep and Goat Research Journal* **18**: 83–88.

Turner H N. 1982. Origins of the CSIRO Booroola. pp. 1-7 in 'The Booroola Merino: proceedings of a workshop held in Armidale, New South Wales, 24-25 August 1980', ed. by L. R. Piper, B. M. Bindon and R. D. Nethery. CSIRO, Melbourne, Australia.

Visscher A H, Dijkstra M, Lord E A, Suss R, Rosler H J, Heylen K and Veerkamp R F. 2000. Maternal and lamb carrier effects of the Booroola gene on food intake, growth and carcass quality of male lambs. *Animal Science* **71**: 209–17.

Visscher A H. 2009. The effect of Booroola gene on meat production efficiency in Texel sheep. 'Proceedings of the Helen Newton Turner Memorial International Workshop on using the *FecB* (Booroola) gene in sheep breeding programs'. (Eds) S. Walkden-Brown, C. Nimbkar, J. van der Werf and V. Gupta. pp. 202. Pune, India.

Walkden-Brown S W, Wolfenden D H and Piper L R. 2009. Biological and economic consequences of introgression of the *FecB* mutation into Merino sheep in Australia. 'Proceedings of the Helen Newton Turner Memorial International Workshop on using the *FecB* (Booroola) gene in sheep breeding programs' (Eds) S. Walkden-Brown, C. Nimbkar, J. Van der Werf, and V. Gupta. pp. 88-98. Pune, India.

Walkden-Brown S W, Wolfenden D H, Charles R J and Maddox J F. 2007. Expression of reproductive and production traits in commercial Merino ewes having 0, 1 or 2 copies of the *FecB* mutation. *'Association of Advancement of Animal Breeding and Genetics"*. Armidale, NSW, Australia (23rd – 26th September 2007) **17**: 426–29.

Walling G A, Dodds K G, Galloway S M, Beattie A E, Lord E A, Lumsden J M, Montgomery G W and McEwan J C. 2000. The consequences of carrying the booroola fecundity (FecB) gene on sheep liveweight. Proceedings of the British Society of Animal Science **2000**: 43.

Willingham T D, Waldron D W and Thompson P V. 2002. Effect of Fec^B allele on birth weight and post-weaning production traits of Rambouillet-Booroola cross wethers. *Sheep and Goat, Wool and Mohair CPR*. pp. 1–6.

Wilson T, Wu X Y, Juengel J L, Ross I K, Lumsden J M, Lord E A, Dodds K G, Walling G A, McEwan J C, O'Connell A R, McNatty K P and Montgomery G W. 2001. Highly prolific booroola sheep have a mutation in the intracellular kinase domain of bone morphogenetic protein 1B receptor (ALK-6) that is expressed in both oocytes and granulose cells. *Biology of Reproduction* **64**: 1225–35.

Young J M, Juengel J L, Dodds K G, Laird M, Dearden P K, McNeilly A S, McNatty K P, and Wilson T. 2008. The activin receptor like kinase 6 Booroola mutation enhances suppressive effects of bone morphogenetic protein 2 (BMP2), BMP4, BMP6, and growth and differentiation factor-9 on FSH release from ovine pituitary cell culture. *Journal of Endocrinology* **196**: 251–61.

Zhou S W, Yu H H, Zhao X E, Cai B, Ding Q, Huang Y, Li Y X, Li Y, Niu Y Y and Wang X L. 2018. Generation of gene-edited sheep with a defined Booroola fecundity gene (FecBB) mutation in bone morphogenetic protein receptor type 1B (BMPR1B) via clustered regularly interspaced short palindromic repeat (CRISPR)/CRISPR-associated (Cas) 9. *Reproduction Fertility Development* **30**: 1616–21.

Zhou S, Ding Y, Liu J, Liu Y, Zhao X, Li G, Zhang C, Li C, Wang X, Kalds P, Gao Y, Zong B, Huang X, Huang S, Yu H, Kou Q, Bjoern P, Huang X, Wang X, Ma B and Chen Y. 2020. Highly efficient generation of sheep with a defined $FecB^B$ mutation via adenine base editing. *Genetics Selection Evolution* **52**: 35.

Zuo B Y, Qian H G, Wang Z Y, Wang X, Nisa N, Bayier A, Ying S J, Hu X L, Gong C H, Guo Z Q and Wang F. 2013. A study on BMPR-IB genes of Bayanbulak sheep, *Asian Australasian Journal of Animal Sciences* **26**: 36–42.