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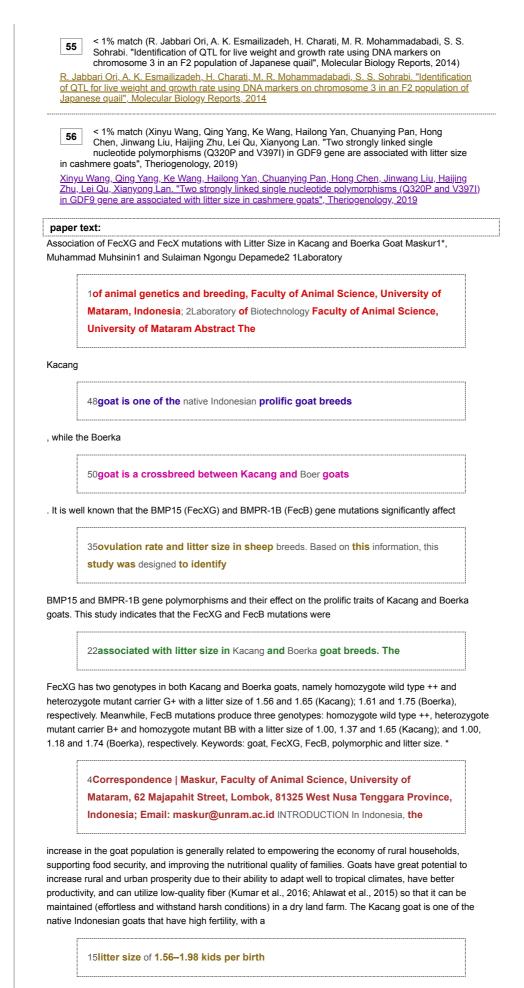
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, 52.2% for twins, and 2.6% for triplets (Pamungkas et al., 2009). While the Boerka goat is a hybrid goat resulting from a cross between Kacang and Boer goat. Boerka goats have the potential to be developed as meat-producing goats because of their better growth and meat quality. Boerka goats have a birth weight of 2.6-2.8 kg with a weaning weight of 10-12 kg, while the birth weight of Kacang goats was 1.6-1.8 kg with a

weaning weight of 6-8 kg. Boerka goats also have prolific characteristics, with a litter size of 1.45-1.54 kids per birth (Mahmilia and Elieser, 2008). Prolific traits are reproductive traits that have high economic value in goats, where high litter size can accelerate goat population growth. The tendency to produce twins or triplets in goats and sheep is the same, and this trait is passed on to their offspring. The genetic mechanism of increasing litter size due to the FecB and FecX mutations has been widely reported. However, prolificacy regulation at the gene level is different in sheep and goats. Mutations in the BMP15 gene increase 37granulosa cells' sensitivity to FSH, leading to accelerated the development of follicular and early ovulation of small follicles , thereby increasing ovulation in ewes (Moore and Shimasaki, 72005). The BMP receptor (BMPR) is expressed by oocytes and granulosa cells and then 10binds to BMP15. The BMPR-1B gene mutation 7has an additive effect on the rate of ovulation (Pramod et al., 2013) and increases the ovulation rate by one copy (Guo et al., 2018). As in sheep, the genetics of prolificacy has also been studied extensively in goats. Several studies have shown 12that the BMP15 gene is also the primary gene that regulates prolificacy in goats, such as 49in Jining Gray goats (Chu et al., 2007), Beetal and Teddy goats (Islam et al., 2019), Funiu 18white goats (Wang et al., 2011), and Markhoz goats (Ghoreishi et al ., 2019). Polymorphism in the BMPR-1B gene was also reported to be associated with prolific traits 15in Black Bengal goats (Polley et al., 2009), Beetal, and Teddy goats (Islam et al., 2019). Contrary, 32Hua et al. (2008) reported none of the FecB and FecX polymorphism in 38prolific goat breeds such as Boer, Haimen, Huanghuai, Nubi and Matou . Based on the abovementioned, the mechanism and regulation pathways of fecundity genes in prolific goats are not clear, so further study is still needed 53in more breeds and a large sample size of a goat. 40Litter size is a reproductive trait with low heritability in goats and is regulated by more than one gene

. Therefore, it was crucial to provide scientific information for designing a set of DNA

52markers that can be useful for marker-assisted selection (MAS

) in Kacang and Boerka goats. MATERIAL AND METHOD Experimental animals and DNA isolation The total sample was 211 female goats, consisting of 111 Boerka and 100 Kacang goats. All samples were collected at PT. Sadhana Arif Nusa, East Lombok, West Nusa Tenggara, Indonesia. The number of kids for every birth and the average litter size

2of the first three parities for each ewe was recorded and used for association analysis

. Blood samples were collected from each animal using a K2EDTA Venoject tube and preserved at -25°C. The Genomic DNA extraction was performed according to the Genomic DNA Mini Kit Geneid procedure. PCR amplification and Genotyping Based on the Ovis aries genbank database (GenBank access code: NC_022322), two pairs of PCR

21primers were designed using Primer 3.0 software and the published nucleotide sequence of the caprine gene

. The forward and reverse primers for

11exon 2 of BMP15 and exon 6 of BMPR1B genes

are presented in table 1. DNA amplification was carried out in the Nexus Mastercycler PCR machine with a 15 µl

39reaction mixture consisting of 1 µl DNA, 0.5 µl Primers

, 6.25 µl MyTaq HS Red Mix, 2x and 7.25 µl Water (dH2O). Amplification conditions were as follows: predenaturation temperature conditions of

595 oC for 5 minutes, followed by 35 cycles for the denaturation step at 95 oC for 10 s, annealing at 60 oC for 20 s, and elongation at 72 oC for 30 s; with the final elongation stage at 72 oC for 5

minutes in one cycle. About 5

).

 $27 \mu l$ of each PCR product were digested separately with Hinf1 10 U

for BMP15 and Avall 10 U for BMPR-1B at 37 °C overnight. The

36DNA fragments were separated by 2.5% agarose gel electrophoresis and visualized

in an Alphalmager (Alpha Innotech Corporation, USA). Data analysis The genotypes and alleles frequency, heterozygosity, polymorphism information content, and

47Hardy-Weinberg equilibrium were examined using Popgene version 1.31

software. SNP position determination was corrected to Ensembl's DNA sequence using the MEGA-X program (ENSCHIG00000024611). The association of genotypes with the litter size of Kacang and Boerka goats was

29analyzed using the GLM (General Linear Model) procedure with SAS 9.1.3 software (SAS Institute, Cary, NC, USA

3The model applied was: Yiklm = μ + Ci + Bk + (BC)ik+ SI + Eiklm Where, Yiklm is the trait measured on each of the iklmth animals; μ is the overall population mean; Ci is the fixed effect of the ith combined genotype; Bk is the fixed effect of the kth breed; (BC)ik is the interaction between the ith and the kth; S1 is the fixed effect of the lth sire, and Eiklm is the random error

. RESULT AND DISCUSSION Polymorphism of BMP15 gene in Kacang and Boerka Goat Amplifying the BMP15 gene in Kacang and Boerka goats produced DNA fragments (PCR products) with a length of 141 bp (Figure 1). Mutation

20of the BMP15 gene was identified by the RFLP method using the

Hinf1 restriction enzyme with the G|ANTC cleavage site (Figure 2). The wild type of the exon 2 BMP15 gene sequence has a cleavage site for the Hinf1 enzyme that produces alleles with sizes of 111 bp and 30 bp (+ allele), respectively. The C/T transition mutation caused a change in the cleavage site of the Hinf1 enzyme at position 718 (

27c.718C>T) of the BMP-15 gene, which resulted in

a mutant allele (G allele) with a size of 141 bp. Identification of allele and genotype of the BMP15 gene using the method of RFLP- Hinf1 resulted in

2two alleles, namely + (wild type) and G (mutant type) allele with two genotypes ++ (homozygote wild type) and

G+ (heterozygote mutant carrier), while the genotype homozygote mutant GG was not identified on Kacang and Boerka goats (Figure 2). The allelic and genotypic frequency distributions indicate

10a highly contrasting difference (P<0.01). The

+ allele was significantly higher

11than the G allele, and the genotype ++ was significantly higher than the

G+ in

32the two goat breeds (Table 2). The presence of

polymorphic sites for

18exon 2 of the BMP15 gene has been published in several breeds

of goats, such as Jining Grey (Chu

17et al., 2007); White Goat of Guizhou (Ran et al., 2009); Funiu white and Taihang black (Wang et al., 2011); Beetal and Teddy goats (Islam et al

., 2019). In this study, the homozygous mutant GG did not find in the Kacang and Boerka goat population. Similarly, homozygous mutant GG also was not found in several goat breeds, such as Markhoz goats (

19Ghoreishi et al., 2019), Teddy goat (Islam et al., 2019), Taihang black (Wang et al., 2011), and

Jining gray (Chu et al., 2007); and some breeds of sheep, such as the

6Small Tailed Han (Chu et al., 2007), Belclare (Mullen et al., 2013), Barki and Rahmani (El- Seedy et al ., 2017), six Egyptian sheep breeds (Saleh et al. 2020), and Lombok Fat Tail (Maskur et al., 2016). The Possible reasons need to be explained that no GG ewes were observed in the present study. A tendency towards accumulating and losing certain genotypes could be due to intensive selection. GG ewes may exist in the Kacang and Boerka breeds, but this research used experimental ewes with a litter record, so all infertile ewes were excluded. Another possible reason that GG ewes may not exist in the Kacang and Boerka breeds is that there are no reports of infertility among Kacang and Boerka goats, as in Belclare sheep. Polymorphism of BMPR-1B gene in Kacang and Boerka Goat Amplifying the BMPR-1B gene in Kacang and Boerka goats produced DNA sequences with a length of 140 bp. The

54wild type of the BMPR-1B gene exon

6 sequence has not a cleavage site for the Avall restriction enzyme, so

10the wild-type of this allele is 140 bp

(+). Mutations at this locus convert

2adenine bases into guanine (A/G transition) at the base

position 746 coding regions of the BMPR-1B gene (c.746A>G). This mutation causes the formation of a cleavage site for the AvaII restriction enzyme (G|GACC), so the digestion produces mutant alleles measuring 110 and 30 bp (B) in length. Identification of allele and genotype

10of the BMPR-1B gene using the

method of RFLP- Avall resulted in two alleles, namely mutant B (110 bp and 30 bp) and wild + allele (140 bp), with three genotypes ++ (homozygote wild type), B+ (heterozygote mutant carrier), and BB (homozygote mutant) (Figure 4). The allelic and genotypic frequency distributions indicate a highly contrasting difference (

14P<0.01). The frequency of the wild + allele was significantly higher than

the mutant B allele, and the genotypic ++ was significantly higher than B+ and BB in the two goats breed (Table 3). However, the previous research in several sheep breeds indicates the abundance of mutant alleles compared to wild alleles, such as in prolific

6Garole sheep (Polley et al., 2010); Indonesian fat-tailed sheep (Maskur et al., 2016); Small-Tail Han (Chu et al., 2007; Wen et al., 2021); and Bayanbulak sheep (Zuo et al

., 2013). Similar to this study,

16the FecB mutation has been previously found in several goat breeds

, such as

11Black Bengal (Polley et al., 2009), Markhoz (Shokrollahi and Morammazi, 2018

), Beetal and Teddy goats (Islam et al., 2019). In contrast, in some other goat breeds, it has not been found, such as the Rayini goats of Iran (

42Gazooei et al., 2013), the prolific Raighar (Palai et al., 2013

), the Indian Berari and Surti goat (Sharma et al. 2016; Dangar et al., 2019), and some Egypt

8sheep breeds (Abulyazid et al., 2011; El-Seedy et al., 2017; Saleh et al

., 2020). The possible reasons for the differences between the results obtained from different breeds may be due to: (1) the accumulation of certain genotypes and alleles as a result of intensive selection, (2) the

possibility of inbreeding, and (3) the possibility of previous genes introgression as a breeding strategy. Genetic Diversity Within the Goat Breeds The genetic index describes a population's genetic diversity by

28the number of alleles, observed heterozygosity (Ho), expected heterozygosity (He), and Polymorphic Information Content (PIC) values

as basic

1information for individual and population discrimination (Seo et al., 2016

). Data in table 4 indicate a genotypic imbalance in the two goat populations where the observed heterozygosity was significantly different from the Hardy-Weinberg expectation agreement. In this study, the low level of Ho and He value revealed low genetic diversity in the two goat populations. The occurrence of heterozygosity deficits in the population is caused by selection pressure at certain loci and inbreeding. The PIC value of exon 2

24of the BMP15 gene in both Kacang and Boerka goat breeds was

0.211 and 0.221, while exon 6 of BMPR1B was 0.170 and 131, respectively. Base on

1Bolstein et al. (1980), the PIC level classified as highly (PIC > 0.50), reasonably (0.50 > PIC > 0.25), and slightly (PIC < 0.25) informative. Thus

, in recent research, the PIC value in both BMP15 and BMPR1B was classified as

55slightly informative (PIC < 0.25). Association of The

FecXG and FecB mutations with

41Litter Size in the Goat Breeds The FecXG (c.718C>T) and FecB (c.746A>G) mutations

were investigated as potential gene candidates for prolificacy in Indonesian Kacang and Boerka goats. The mutations

7and their effect on ovulation rates and/or litter size were initially found in sheep

and subsequently identified in other species, such as goats.

16On the other side, several previous investigations in different breeds of

sheep and goats found no FecB and FecXG mutations and/or

19their association with litter size. The influence of The

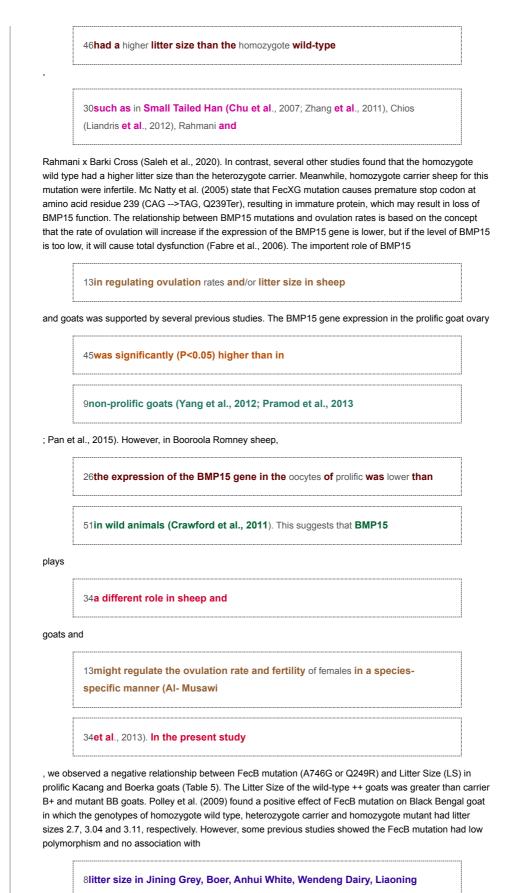
FecXG (c.718C>T) mutation on goat litter size is apparent from the data of this study (Table 5). We found two genotypes in both goat breeds, namely homozygote wild type ++ and heterozygote carrier G+, in which the G+ had a higher number of kids than the ++ genotype. These findings are similar to the previous study

23in Jining Grey goats, in which the heterozygote carrier AB had 1.13 kids more than the homozygote AA

0.01) (Chu et al., 2007). Conversely, some other researchers observed that the homozygote mutant goats

43had the highest number of kids, followed by the

heterozygote carrier and homozygote wild-types, such as Beetal and Teddy goats (Islam et al., 2019), Anglo-Nubian (Abdel-Rahman et al., 2013), Funiu white and Taihang black (Wang et al., 2011). In sheep breeds, some previous studies also confirmed the heterozygote carrier genotype for BMP-15



Cashmere

, Barbari, Malabari, Osmanabadi, and Ganjam goats (Ahlawat

9et al., 2014; Chu et al., 2010). The different genetic effects of

these mutations are possibly caused by the intense selection pressure on the population resulting in the accumulation of certain genotypes.

12This In turn would affect the effective population size in the goat genotype

group and will have an impact on the results of the significant association

analysis. Another possible reason is that the BMPR-1B gene expression may vary between breeds and environmental conditions or due to the interactions between breeds and the environment (Fogerty, 2008). In sheep breeds, some researchers have confirmed that

14the FecB mutation has an effect on ovulation rate and/or litter

sizes, such as Dorset, Mongolian,

31Small-Tail Han, Hu and Bayanbulak sheep (China: Jia et al., 2019; Wen et al.,

2021; Wang et al

., 2018; Zuo et al., 2013); Garole, Nilagiri, Nellore and Deccani sheep (India: Polley

33et al., 2010; Praveena et al., 2017; Chaudhari et al., 2019); Mehraban and Kalehkoohi (Iran: Abdoli et al

.,

92013; Talebi et al., 2018; Mahdavi et al., 2014). The important role of

FecB mutations in the regulation of sheep reproduction has been confirmed in several previous studies. The FecB mutation reduces the BMPR-IB inhibitory effect on granulosa cell steroidogenesis so that they

2are more sensitive to FSH; thus, the cell division becomes more active, leading to

the maturation and ovulation of multiple ovarian follicles (Fabre et al., 2006). The basic concept of the prolific nature is that an increased ovulation rate leads to a more significant

2number of ovulated oocytes and if fertilization occurs and

the parent is able to maintain a viable embryo,

2it will be followed by the birth of more than one kid (Wilson et al., 2001). CONCLUSION

According to these results, we can state that BMP15 and BMPR1B gene was polymorphic and significantly affected on litter size in Kacang and Boerka goats.

25The results of this study will hopefully provide a basis for the development of

56marker-assisted selection (MAS) for goat breeding programs in

the future. However, our study has limitations on the effective population size of each genotype group in the test goats, which will impact the association analysis results. Therefore, further investigations

44on a large number of animals and balanced populations are needed to

confirm the association of BMP15 and BMPR1B genes with increased prolificacy in Kacang and Boerka goats. Acknowledgment The University of Mataram Research Grant funded this research with contract number: 2832/UN18.L1/PP2020. The greatest appreciation to the Rector of the

1University of Mataram for the support of this research. Novelty Statement The

Vet, Puslitbangnak Deptan, Bogor, Hal, 391- 394, Maskur M, Tapaul R, Kasip L (2016), Genetic polymorphism of bone morphogenetic protein receptor 1B (BMPR-1B) gene and its association with litter size in Indonesian fat-Tailed sheep. African J. Biotech., 15(25): 1315-1319. Mc Natty KP, Juengel JL, Reader KL, Lun S, Myllymaa S, Lawrence SB (2005). Bone morphogenetic protein 15 and growth di_erentiation factor 9 cooperate to regulate granulosa cell function in ruminants. Reproduction. 129: 481-487. [CrossRef] [PubMed] Moore RK and Shimasaki S (2005). Molecular biology and physiological role of the oocyte factor, BMP-15. Mol. Cell.Endocrinol. 234: 67-73. Mullen MPHJ, Howard DJ, Powell R (2013). Investigation of prolific sheep from UK and Ireland for evidence on origin of the mutations in BMP15 (FecXG, FecXB) and GDF9 (FecGH) in Belclare and Cambridge sheep. PLoS ONE. 8. Palai TK, Bisoi PC, Maity A, Behera PC, Sahoo G, Polley S, De S (2013). 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1. The word association in the title should be replaced with the word identification

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<u>Wouobeng, Patrick, Kouam Simo, Jaures et al. "Polymorphism of Prolificacy</u> <u>Genes (BMP15, BMPR 1B and GDF9), in the Native Goat (Capra hircus) of</u> <u>Cameroon", 'University of Tlemcen', 2019</u>

Identification of FecXG and FecX mutations and End Match its association with Litter Size in End Match Kacang and End Match Boerka Goat Maskur1*, Muhammad Muhsinin1 and Sulaiman Ngongu Depamede2 1Laboratory of animal genetics and breeding, Faculty of Animal Science, University of Mataram, Indonesia End Match; 2Laboratory of End Match Biotechnology Faculty of Animal Science, University of Mataram Abstract The End Match Kacang goat is one of Indonesia's prolific native goat breeds, while the Boerka goat is a crossbreed between Kacang and End Match Boer goats End Match. It is widely known that the ovulation rate and litter size in sheep breeds End Match are significantly impacted by the BMP15 (FecXG) and BMPR-1B (FecB) gene alterations. Based on this knowledge, the study's objective was to determine the presence of BMP15 and BMPR-1B gene polymorphisms and how they affected the prolific traits of Kacang and Boerka goats. This study indicates that the FecXG and FecB mutations were associated with litter size in End Match Kacang and End Match Boerka goat breeds. The End Match FecXG has two genotypes in both Kacang and Boerka goats, namely homozygote wild type ++ and heterozygote mutant carrier G+ with a litter size of 1.56 and 1.65 (Kacang); 1.61 and 1.75 (Boerka), respectively. Meanwhile, FecB mutations produce three genotypes: homozygote wild type ++, heterozygote mutant carrier B+ and homozygote mutant BB with a litter size of 1.00, 1.37, and 1.65 (Kacang); and 1.00, 1.18, and 1.74 (Boerka), respectively. Keywords: goat, FecXG, FecB, polymorphic and litter size. *Correspondence | Maskur, Faculty of Animal Science, University of Mataram, 62 Majapahit Street, Lombok, 81325 West Nusa Tenggara Province, Indonesia; Email: maskur@unram.ac.id End Match INTRODUCTION In Indonesia, the End Match increase in the goat population is generally related to empowering the economy of rural households, supporting food security, and improving the nutritional quality of families. Goats have great potential to increase rural and urban prosperity due to their ability to adapt well to tropical climates, have better productivity, and can utilize low-quality fiber (Kumar et al., 2016; Ahlawat et al., 2015) so that it can be effortlessly maintained in a dry land farm. The Kacang goat is one of the native Indonesian goats that have high fertility, with a litter size End Match of 1.56–1.98 kids per birth End Match, 52.2% for twins, and 2.6% for triplets (Pamungkas et al., 2009). While the Boerka goat is a hybrid goat resulting from a cross between Kacang and Boer goat. As a hybrid breed, Boerka goats have the potential to be developed as meatproducing goats because of their better growth and meat quality. Boerka goats have a birth weight of 2.6-2.8 kg with a weaning weight of 10-12 kg, while the birth weight of Kacang goats was 1.6-1.8 kg with a weaning weight of 6-8 kg. Boerka goats also have prolific characteristics, with a litter size of 1.45–1.54 kids per birth (Mahmilia and Elieser, 2008). Prolific traits are reproductive traits that have high economic value in goats, where high litter size can accelerate goat population growth. The tendency

to produce twins or triplets in goats and sheep is the same, and this trait is passed on to their offspring. The genetic mechanism of increasing litter size due to the FecB and FecX mutations has been widely reported. However, prolificacy regulation at the gene level is different in sheep and goats. Mutations in the BMP15 gene make granulosa cells more sensitive to FSH, accelerating the formation of follicular and early ovulation of tiny follicles, thereby increasing ovulation in ewes (Moore and Shimasaki, 2005). Granulosa cells and oocytes express the BMP receptor (BMPR) and End Match then bind to BMP15. The ovulation rate is enhanced by one copy due to an additive effect of the BMPR-1B gene mutation (Pramod et al., 2013; Guo et al., 2018). As in sheep, the genetics of prolificacy has also been studied extensively in goats. Several studies have shown that the BMP15 gene is End Match also the primary gene that End Match regulates prolificacy End Match in goats, such as in Funiu white (Wang et al., 2011 End Match), Jining Gray (Chu et al End Match., 2007), Beetal and Teddy (Islam et al End Match., 2019), and End Match Markhoz goats End Match (Ghoreishi et al End Match., 2019). Polymorphism in the BMPR-1B gene was also reported to be associated with prolific traits in Black Bengal (Polley et al., 2009) End Match), Beetal, and End Match Teddy goats End Match (Islam et a End Match., 2019). On the contrary, Hua et al. (2008) showed none of the FecB and FecX End Match polymorphism in prolific PEnd Match goat breeds PEnd Match, including Haimen, Huanghuai, Boer, Nubi and Matou. Based on the abovementioned, the mechanism and regulation pathways of fecundity genes in prolific goats are not clear, so additional study is still required in various breeds and a large sample size of a goat. In goats, litter size is a End Match reproductive trait with low heritability End Match and is regulated by more than one gene. Therefore, it is crucial to provide scientific information for designing a set of DNA markers that End Match can be useful End Match for marker-assisted selection (MAS End Match) in Kacang and Boerka goats. MATERIAL AND End Match METHOD Experimental animals and DNA isolation End Match The experiments were End Match carried out with a total sample was 211 female goats, consisting of 111 Boerka and 100 Kacang goats. All samples were collected at PT. Sadhana Arif Nusa, East Lombok, West Nusa Tenggara, Indonesia. For association analysis, the number of kids for every birth and the average litter size for each ewe of the first three parities End Match were recorded End Match. Blood samples were collected from each animal using a K2EDTA Venoject tube and preserved at -25°C. The Genomic DNA End Match extraction was performed according to the Genomic DNA Mini Kit Geneid procedure. PCR amplification and Genotyping Primer 3.0 software was used to design End Match two pairs of PCR primers based on the End Match Ovis aries genbank database (GenBank access code: NC_022322) and the published nucleotide sequence of the caprine gene End Match. The forward and reverse primers for exon 2 of BMP15 and exon End Match 6 of End Match BMPR1B genes End Match are presented in table 1. DNA amplification was carried out in the Nexus Mastercycler PCR machine with a reaction volume of a 15 μ l consisted 1 μ l DNA, 0.5 µl Primers End Match, 6.25 µl End Match MyTaq HS Red Mix, 2x and 7.25 µl Water (dH2O). Amplification conditions were as follows End Match: pre-denaturation End Match conditions for 5 End Match minutes at 95 End Match oC, followed by End Match 35 cycles of denaturation End Match step at 95 oC for End Match 10 s, annealing at 60 oC for End Match 20 s, and elongation at 72 oC for 30 s End Match; with the final elongation End Match stage at 72 oC for End Match 5 minutes in one cycle. About 5 µl of each PCR product End Match were digested End Match separately with End Match Hinf1 10 U End Match for BMP15 and AvaII 10 U for BMPR-1B at 37 °C overnight. The digested product was separated End Match by 2.5% agarose gel End Match electrophoresis and visualized in an AlphaImager (Alpha Innotech Corporation, USA). Data analysis Popgene version 1.31 software was used

to End Match investigate the genotype End Match and allele frequencies, heterozygosity, polymorphism information content End Match, and Hardy-Weinberg equilibrium. SNP position determination was corrected to Ensembl's DNA sequence using the MEGA-X program (ENSCHIG00000024611). The association of genotypes with End Match the litter size of End Match Kacang and Boerka goats End Match was examined using the General Linear Model procedure End Match with SAS 9.1.3 software (SAS Institute, Cary, NC, USA). The End Match linear model applied was End Match: Yiklm = μ + Ci + Bk + (BC)ik+ SI + Eiklm Where, Yiklm End Match is the trait End Match observation of the iklmth End Match animals; μ is the overall mean End Match; Ci is the End Match genotype effect of the End Match ith; Bk is the End Match breed effect End Match of the End Match kth; (BC)GNRH1 and GDF9 genes and their association analysis with litter size", Animal Genetics, 2013.">ik is the interaction between the ith and the kth End Match; S1 GNRH1 and GDF9 genes and their association analysis with litter size", Animal Genetics, 2013.">is the End Match sire GNRH1 and GDF9 genes and their association analysis with litter size", Animal Genetics, 2013.">effect End Match of GNRH1 and GDF9 genes and their association analysis with litter size", Animal Genetics, 2013.">the lth, and End Match Eiklm GNRH1 and GDF9 genes and their association analysis with litter size", Animal Genetics, 2013.">is the random error End Match. RESULT AND DISCUSSION Polymorphism of BMP15 gene in Kacang and Boerka Goat Amplifying the BMP15 gene in Kacang and Boerka goats produced DNA fragments (PCR products) with a length of 141 bp (Figure 1). The BMP15 gene mutation was identified by the RFLP method using the Hinf1 restriction enzyme with the G|ANTC cleavage site (Figure 2). The wild type of the exon 2 BMP15 gene sequence has a cleavage site for the Hinf1 enzyme that produces alleles with sizes of 111 bp and 30 bp (+ allele), respectively. The C/T transition mutation caused a change in the cleavage site of the HinfI enzyme at position 718 (c.718C>T) of the BMP-15 gene End Match, which resulted in End Match a mutant allele (G allele) with a size of 141 bp. Identification of allele and genotype of the BMP15 gene using the method of RFLP- Hinf1 resulted in wild type + and mutant type G allele with homozygote wild type ++ and heterozygote mutant carrier G+ genotypes, while the homozygote mutant GG genotype was not identified on Kacang and Boerka goats (Figure 2). The allelic and genotypic frequency distributions indicate a very contrasting difference (P<0.01). In the End Match two goat End Match breeds, the End Match genotype ++ was significantly End Match higher than the G+, and the + allele was significantly higher than the End Match G allele End Match (Table 2). The presence of polymorphic sites for exon 2 of End Match the BMP15 gene End Match has been published in End Match various breeds of End Match goats, such as Jining Grey (Chu et al., 2007 End Match); Guizhou White (Ran et al., 2009 \searrow End Match); Taihang black and Funiu white (Wang et al., 2011 End Match); Beetal and End Match Teddy goats (Islam et al End Match., 2019). In this End Match study, the End Match homozygous mutant GG was not found in the Kacang and Boerka goat populations. Similarly, homozygous mutant GG also was not found in several goat breeds, such as Teddy goats (Islam et al., 2019), Markhoz goats (Ghoreishi et al., 2019), Taihang black (Wang et al., 2011), and End Match Jining gray (Chu et al End Match., 2007); and some breeds of sheep, including the Small Tailed Han (Chu et al., 2007 End Match), Belclare (Mullen_et al End Match., 2013), Barki and End Match Rahmani (El-Seedy et al) End Match., 2017), six Egyptian sheep breeds (Saleh et al. 2020), and Lombok Fat Tail (Maskur et al., 2016). The Possible reasons need to be explained that no GG ewes were observed in the present study. A tendency towards accumulating and losing certain genotypes could be due to intensive selection. GG ewes may exist in the Kacang and Boerka breeds, but this research used experimental ewes with a litter record, so

all infertile ewes were excluded. Another possible reason that GG ewes may not exist in the Kacang and Boerka breeds is that there are no reports of infertility among Kacang and Boerka goats, as in Belclare sheep. Polymorphism of BMPR-1B gene in Kacang and Boerka Goat Amplifying the BMPR-1B gene in Kacang and Boerka goats produced DNA sequences with a length of 140 bp. The wild type sequence of exon 6 of the BMPR-1B gene End Match has no cleavage site for the AvaII restriction enzyme, so the wild type allele is 140 bp End Match (+). Mutations at this locus are transition mutations that End Match convert adenine End Match into guanine at the End Match base position End Match 746 coding regions of the BMPR-1B gene (c.746A>G). These mutations cause the formation of a cleavage site for the AvaII restriction enzyme (G|GACC), so the digestion produces mutant alleles measuring 110 and 30 bp (B) in length. Identification of allele and genotype using the method of RFLP-AvaII resulted in two alleles, namely mutant B (110 bp and 30 bp) and wild + allele (140 bp), with three genotypes ++ (homozygote wild type), B+ (heterozygote mutant carrier), and BB (homozygote mutant) (Figure 4). The allelic and genotypic frequency distributions indicate a highly contrasting difference (P<0.01). The End Match frequency of the End Match wild + allele was significantly higher than End Match the mutant B allele, and the genotypic ++ was significantly higher than B+ and BB in the two goats breed (Table 3). However, the previous research in several sheep breeds indicates the abundance of mutant alleles compared to wild alleles, such as in prolific Garole (Polley et al., 2010); Indonesian fat-tailed (Maskur et a) End Match., 2016); Small 戻 End Match-Tail Han (Chu et al 💭 End Match., 2007; Wen et al End Match., 2021); and Bayanbulak End Match sheep (Zuo et al., 2013 End Match). Similar to this study, the FecB mutation has been End Match previously found in several End Match goat breeds End Match, including Black Bengal (Polley et al., 2009 End Match), Markhoz (Shokrollahi and Morammazi, 2018 End Match), Beetal and Teddy goats (Islam et al., 2019). In contrast, it has not been found in some other goat breeds, including the Rayini goats of Iran (Gazooei et al., 2013 End Match), the prolific Raighar (Palai et al., 2013), the Indian Berari and Surti goat (Sharma et al. 2016; Dangar et al., 2019), and some Egypt sheep breeds End Match (Abulyazid et al End Match., 2011; El End Match-Seedy et al End Match., 2017; Saleh et al End Match., 2020). The possible reasons for the differences between the results obtained from different breeds may be due to: (1) the accumulation of certain genotypes and alleles as a result of intensive selection, (2) the possibility of inbreeding, and (3) the possibility of previous genes introgression as a breeding strategy. Genetic Diversity Within the End Match Goat Breeds End Match The genetic diversity End Match of a population is End Match represented by the number of alleles End Match, expected heterozygosity (He End Match), observed heterozygosity (Ho), and End Match Polymorphic Information Content (PIC) values End Match as the fundamental data for individual and population discrimination (Seo et al., 2016 End Match). Data in table 4 indicate a genotypic imbalance in the two goat populations where the observed heterozygosity was significantly different from the Hardy-Weinberg expectation agreement. In this study, the low level of Ho and He values revealed low genetic diversity in the two goat populations. The occurrence of heterozygosity deficits in the population is caused by selection pressure at certain loci and inbreeding. The PIC value of the FecXG (c.718C>T) in both Kacang and Boerka goat breeds was 0.211 and 0.221, while FecB (c.746A>G) was 0.170 and 131, respectively. Base on Bolstein et al. (1980), the PIC End Match level classified as highly (PIC > 0.50), reasonably End Match (0.50 > PIC > 0 End Match.25), and slightly (PIC < 0.25) informative. Thus End Match, in recent research, the PIC value in both BMP15 and BMPR1B was classified as slightly informative (PIC < 0.25 End Match). Association of The End Match

FecXG and FecB mutations with Litter Size in the Goat Breeds The End Match mutations of FecXG (c.718C>T) and FecB (c.746A>G) were investigated as potential gene candidates for prolificacy in Indonesian Kacang and Boerka goats. The mutations and their End Match influence on litter size and ovulation rates End Match were initially found in sheeps and subsequently identified in other species, such as goats. On the other hand, no FecB and FecXG mutations and End Match/or their association with litter size End Match were detected in End Match earlier studies in various breeds of sheep End Match and goats. The influence of The End Match FecXG (c.718C>T) mutation on goat litter size is apparent from the data of this study (Table 5). We found two genotypes in both goat breeds, namely homozygote wild type ++ and heterozygote carrier G+, in which the G + had a higher number of kids than the ++ genotype. These findings are similar to the previous study done on Jining Grey goats, in which the heterozygote carrier AB had 1.13 more offspring than the homozygote AA (p < 0.01) (Chu et al., 2007). Conversely, some other researchers observed that the homozygote mutant goats had the most offspring, followed by the heterozygote carrier and homozygote wildtypes, such as Beetal and Teddy goats (Islam et al., 2019), Anglo-Nubian (Abdel-Rahman et al., 2013), Funiu white and Taihang black (Wang et al., 2011). In some sheep breeds, such as the Small Tailed Han (Chu et al., 2007 End Match; Zhang et al End Match., 2011), the End Match Chios (Liandris et al End Match., 2012), the Rahmani, and the Rahmani x Barki Cross (Saleh et al., 2020), previous studies also demonstrated that the heterozygote carrier genotype for BMP-15 had a larger litter size than the End Match homozygote wild-type End Match. In contrast, several other studies found that the homozygote wild type had a higher litter size than the heterozygote carrier. Meanwhile, homozygote carrier sheeps for this mutation were infertile. Mc Natty et al. (2005) state that FecXG mutation causes premature stop codon at amino acid residue 239 (CAG -->TAG, Q239Ter), resulting in immature protein, which may result in loss of BMP15 function. The relationship between BMP15 mutations and ovulation rates is based on the concept that the rate of ovulation will increase if the expression of the BMP15 gene is lower, but if the level of BMP15 is too low, it will cause total dysfunction (Fabre et al., 2006). The important role of BMP15 in modulating litter size and End Match the rate of End Match ovulation in End Match sheeps and goats was supported by several previous studies. The BMP15 gene expression was significantly (P<0.05) higher in End Match the prolific goat End Match than in non-prolific goats' ovaries (Yang et al., 2012 End Match; Pramod et al., 2013 End Match; Pan et al., 2015 End Match). However, Crawford et al End Match. (2011) found that End Match the BMP15 End Match gene expression in the End Match oocytes of prolific was lower End Match than in End Match wild Booroola Romney sheeps. This finding suggests that BMP15 plays a distinct role in goats and sheep, and that it may regulate female fertility and ovulation rate in a species-specific manner (Al- Musawi et al., 2013 End Match). In the current research, we observed a negative relationship between FecB mutation (A746G or Q249R) and Litter Size (LS) in prolific Kacang and Boerka goats (Table 5). The Litter Size of End Match the wild-type End Match ++ goats was End Match greater than End Match carrier B+ and mutant BB goats. Polley et al. (2009) found a positive effect of FecB mutation on Black Bengal goats in which the genotypes of homozygote wild type, heterozygote carrier and homozygote mutant had litter sizes of 2.7, 3.04, and 3.11, respectively. However, some previous studies showed the FecB mutation had low polymorphism and no association with litter size in Anhui White, Wendeng Dairy, Jining Grey, Boer, Liaoning Cashmere, Barbari, Malabari, Osmanabadi, and Ganjam goats (Ahlawat et al., 2014; Chu et al., 2010). The different genetic impacts of these mutations are possibly caused by the intense selection pressure on the population resulting in the accumulation of certain genotypes. This in turn would have an impact on

the effective population size End Match in the End Match goat genotype group and would End Match alter the End Match results of the End Match significant association End Match analysis. Another possible reason is that the BMPR-1B gene expression may vary between breeds and environmental conditions or due to the interactions between breeds and the environment (Fogerty, 2008). In sheep breeds, some researchers have confirmed that the FecB mutation has an effect on ovulation End Match rate and End Match/or litter End Match sizes, such as Dorset, Mongolian, Small-Tail Han End Match, Hu and Bayanbulak sheep (China End Match: Jia et al End Match., 2019; Wen et al End Match., 2021; Wang et al End Match., 2018; Zuo et al., 2013); Garole, Nilagiri, Nellore and Deccani sheep (India: Polley et al., 2010 End Match; Praveena et al End Match., 2017; Chaudhari et al., 2019 End Match); Mehraban and Kalehkoohi (Iran) End Match: Abdoli et al) End Match., 2013 End Match ; Talebi et al End Match., 2018; Mahdavi et al., 2014). The End Match important role of End Match FecB mutations in the regulation of sheep reproduction has been confirmed in several previous studies. The FecB mutation reduces the BMPR-IB inhibitory effect on granulosa cell steroidogenesis so that they are more sensitive to FSH; thus, the End Match cell division becomes more End Match active, leading to End Match the maturation and ovulation of multiple ovarian follicles (Fabre et al., 2006). The basic concept of the prolific nature is that an increased ovulation rate leads to a more significant number of ovulated oocytes and if fertilization occurs and End Match the parent is able to maintain a viable embryo, it will be followed by the birth of more than one End Match kid (Wilson et al., 2001 End Match). 7 CONCLUSION End Match According to these results, we can state that BMP15 and BMPR1B genes were polymorphic and significantly affected the litter size in End Match Kacang and End Match Boerka goats End Match. The results of this study End Match will hopefully provide a basis for the development of End Matchmarker-assisted selection (MAS) for End Match goat breeding End Match programs in End Match the future. However, our study has limitations on the effective population size of each genotype group in the test goats, which will impact the association analysis results. Therefore, further investigations on large and balanced populations are required to confirm the End Match association of End Match BMP15 and BMPR1B genes with increased prolificacy in End Match Kacang and Boerka goats. Acknowledgment The University of Mataram Research Grant funded this research with contract number: 2832/UN18.L1/PP2020. The greatest appreciation to the Rector of the University of Mataram for the support End Match of this research End Match. Novelty Statement The End Match authors declare that the article is original and sourced from unpublished research data. The Faculty of Animal Science University of Mataram's ethics committee granted all the research materials and procedures with registration number: 10/UN18.F2/EC/2021. Author's Contributions Maskur was responsible for designing, analyzing, interpreting data, and preparing the manuscript; Muhammad Muhsinin was responsible for phenotypic and genotypic analysis, and preparation of the manuscript; and Sulaiman Ngongu Depamede was responsible for the experiment, laboratory analysis, and article preparation. REFERENCES Abdel-Rahman SM, Mustafa YA, Abd Errasool HA, El-Hanafy AA, El-Maghraby AM (2013). Polymorphism in BMP-15 gene and its association with litter size in Anglo-Nubian goat. Biotechnology in Animal Husbandry. 29(4): 675?683. https://doi.org/10.2298/BAH1304675A Abdoli R, Zamani P, Deljou A, and Rezvan, H (2013). Associations of BMPR-1B and GDF9 genes polymorphisms and secondary protein structure changes with reproduction traits in Mehraban ewes. J.Gene, 524: 296-303. https://doi.org/10.1016/2013.03.133 Abulyazid I, Abdalla M, Sharada H, Saleh H, Hassanin W (2011). Prolificacy detection in Egyptian sheep using RFLP-specific PCR. Egypt Acad J. Biological Sci., 1: 1–4. Ahlawat S,

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