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Identification of Boerka Goats Raised in Bali by using Molecular Analysis of *IGF1* (Insulin-Like Growth Factor 1) Gene

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ABSTRACT

The fulfillment of the lamb demand in Bali, Boerka goats was developed by the local government in 2019. Boerka goats resulting from a cross between male Boer breeds and female Kacang goats are categorized as meat goats and predicted to have good adaptation to unfavorable environments like the Kacang goats and have good meat quality like Boer goats as their parents. The study aims to analyze insulin-like growth factor 1 (*IGF1*) as a gene related to the growth of Boerka goats. A total of 16 Boerka goats from a group of livestock farmers in Sanda village were used as objects of study. The blood samples were taken in a venoject tube filled with EDTA anticoagulant. DNA total was extracted from each sample and subjected to PCR with IFG-1 gene target by using IGF677F 5'-ATTACAAAGCTGCCTGCCCC-'3 and IGF879R 5'-ACCTTACCCGTATGAAAGGAATATACGT-'3 primers. PCR products were then sequenced and analyzed with the MEGA 11 program. Results of the study showed the IFG-1 gene of Boerka goats compose of nucleotides dominated by adenine base guanine (22.3%), and pyrimidine tyrosine (33.9%). In conclusion, Boerka goats raised in Bali genetically share a clade with Ovis aries and Capra malabari with a bootstrap value is 99% as a type of meat and milk goats so that Boerka goats tend to have characteristics and appearance resembling *Ovis aries* and *Capra malabari* goats.

Key words: Boerka goats, IGF1 gene, Bali, Indonesia.

INTRODUCTION

Field observations of goats bred in Bali generally found Kacang and Etawah crossbreed goats. Since 2019, located in Sanda village, Pupuan district, Tabanan regency-Bali, the Boerka goats have been introduced to be new breed as a cross between Kacang goats and Boer goats. As many as 82 females and 12 males Boerka goats were imported from the Research Workshop (Lolit Goat) Sei Putih, Nort Sumatra (Anonymous 2018). As a combination of the two parents, the Boerka goats are expected to has two superior, such as their lamb quality inherited from male Boer and the wide adaptability in limited environments inherited from female Kacang goats (Sellier 2000).

According to a previous study (Suyasa et al. 2023), the Boerka goats bred in Bali have relatively the same body weight and head length as Kacang goats and are smaller than Etawah crossbreed goats (P<0.01). Other variables like chest depth, chest width, chest circumference, left front leg cannon circumference, ear width, tail length, and hip height are also significantly (P<0.01) smaller than Etawah

crossbreed goats. On the other hand, the three types of goats have the same size, namely head width and tail width. Meanwhile, the head height of the Boerka goat was almost the same as the Kacang goat and significantly (P<0.01) different from the Etawah crossbred goat. For body length, the Boerka goat is significantly longer than the Kacang goat, but still shorter than the Etawah crossbreed goat. Meanwhile, the length of the horns of Boerka goats was significantly longer compared to Etawah crossbred and Kacang goats (P<0.01). In terms of shoulder height, Boerka goats have almost the same shoulders as Kacang goats but are still shorter than Etawah crossbreed goats. Based on the morphometry data above, until now, no information has been published about their genetics, especially the IGF1 (insulin-like growth factor 1) gene as one of the important genes that control growth and development of the body (Laron 2001), production attributes and carcass quality (Kader Esen and Esen 2023). As it is known, insulin-like growth factor (IGF) is based of protein that transmit most of the effects of growth hormone (GH), where their structure and functions are similar to insulin but their

Cite This Article as: Suardana IW and Suyasa IN, 2024. Identification of boerka goats raised in bali by using molecular analysis of *IGF1* (insulin-like growth factor 1) gene. International Journal of Veterinary Science 13(5): 550-556. https://doi.org/10.47278/journal.ijvs/2024.131 growth-promoting effects are much stronger. *IGF1* mediates the effect of pituitary GH in protein anabolic and linear growth-promoting. *IGF1* also has a GH-independent growth-stimulating effect, on cartilage cells, and their effect possibly will be optimized by the synergistic action with GH (Laron 2001).

IGF1 is a primary mediator of GH effects. It is known, growth hormone is made in the anterior pituitary gland, and released into the bloodstream. Growth hormone stimulates the liver to produce *IGF1*. Furthermore, *IGF1* stimulates systemic body growth and has growth-promoting effects on almost every cell in the body, such as cartilage, skeletal muscle, bone, liver, kidney, nerve, lung cells, skin, and hematopoietic (Yakar et al. 2002), moreover correlate with the milk and dairy intake of the body (Romo Ventura et al. 2020).

IGF1 levels remain stable in the blood, different from GH levels that fluctuate throughout the day depending on your diet and activity levels. This condition as a consideration of the *IGF1* test is a useful way to find out the normality of the GH in the body (McGuire et al. 1992) as well as to identify the GH deficient (Ibba et al. 2020; Fatani 2023). Based on the Boerka goats as a new strain bred in Bali besides the study about their *IGF1* gene has not been studied yet, the study of the *IGF1* gene of Boerka goats as a genetic marker of growth and compare it with other data that was deposited in Genbank to be interesting to present.

MATERIALS AND METHODS

Ethical Approval

The study protocol has been approved by the Ethics Committee of the Faculty of Veterinary Medicine, University of Udayana vide letter No. B/44/UN14.2.9/PT.01.04/2023.

Blood Collection of the Samples

A total of 2mL blood samples originating from 16 female Boerka goats were used in this study. The blood was taken from the jugular vein of Boerka goats using a 5mL venoject-tube which had been filled with ethylenediaminetetraacetic acid anticoagulant @ 1mg/mL. The samples were then brought in an ice box to the laboratory for the next test.

DNA Extraction

DNA total from the blood samples were extracted using QIAamp DNA Mini Kits (Qiagen) with the procedure according to the manufacturer's instructions (Suardana et al. 2018; Suryawan et al. 2020; Suyasa et al. 2023). Blood sample (100µL) containing EDTA anticoagulant was added 20µL proteinase K and 100µL aquadest in a 1.5mL Eppendorf. The mixtures were then vortexed before being incubated at 56°C for 10min. After that, 200 µL of ethanol (96%) was added, followed by pipetting the mixture to DNAeasy Mini Spin Column. Centrifuged at 8000 rpm for 1min, and discharged the remaining liquid. Replaced with the new one of the collection tubes as a remaining liquid-collection part of the DNAeasy Mini Spin Column. Added 500 µL buffer AW 1, and centrifuged at 800rpm for 1min. Discharged the remaining liquid and replaced the collection tube with the

new one. Added 500 μ L buffer AW2 into the column and centrifuged with 14.000rpm for 3min. Moved the DNAeasy Mini Spin Column to the sterile 1.5mL tube. Added 60 μ L of AE buffer, and waited for 1min, before centrifuging 8000rpm for 1min to dilute the DNA that trapped in the column was ready to use.

Amplification of IGF1 Gene

The *IGF1* gene was amplified using the PCR formula in 25µL reaction volumes containing 12.5µL PCR MyTaq HS Red Mix $2\times$ (Bioline Reagents), 1µL DNA template (300ng/µL), and 2µL of each primer (10pmol/µL) such as IGF677F 5'-ATTACAAAGCTGCCTGCCCC-'3 and IGF879R 5'-

ACCTTACCCGTATGAAAGGAATATACGT-'3 (Mu'in 2008). The *IGF1* gene amplification using Thermocycler Eppendorf Mastercycler personal/PTC 100. The PCR program was conducted with initial DNA denaturation at 94°C for 5min, followed by 30 cycles of denaturation at 94°C for 1min, annealing at 60°C for 30s, and elongation at 72°C for 30s. The PCR was ended with a final extension at 72°C for 5 min. The PCR product was then analyzed in a 1.5% agarose (Gibco BRL) gel. As much as 5µL PCR product was stained with FluoroVue Nucleic Acid solution (5µL/50mL) and then electrophoresis at 100 volts for 30min. The gel was visualized by ultraviolet transillumination and recorded by a digital camera FE-270 7.1 megapixels (Suyasa et al. 2023).

Sequencing and Phylogenetic Analysis

The sequencing of 5 out of 12 *IGF1* genes as representations was conducted using a genetic analyzer (ABI Prism 3130 and 3130 xl GeneticAnalyzer) at 1st BASE Pte Ltd, Singapore through PT. Genetica Science Service, Jakarta with the same primers namely, IGF677F and IGF879R. The sequences were edited in MEGA 11 version software to exclude the PCR primer binding sites. The *IGF1* gene sequences of Boerka goats were then compared against *IGF1* sequences of goats that available in databanks (http://www.ncbi.nlm.nih.gov/) automatically using the BLAST program (Tamura et al. 2021), and the phylogenetic tree was constructed using the arithmetic mean algorithm, and unweighted pair group method (Suardana et al. 2013; Suardana et al. 2015).

RESULTS AND DISCUSSION

Amplification of the *IGF1* gene from Boerka goats raised in Bali was successful, characterized by the detection of a single band at position 249bp (Fig. 1) and the alignment results of the 5 nucleotide sequence of Boerka goats as the representation of all samples were presented in Table 1.

Table 1 shows that of the 254 *IGF1* nucleotide bases compared, many different bases were found between the Boerka goat group and other goat breeds. The *IGF1* alignment shows several substitutions, deletions, or insertions in the alignment DNA. However, specifically for Boerka goats, a mutation was also found at the 31st base from C to A. This mutation is included in the type of transversion mutation, namely the replacement of a pyrimidine nucleotide (T or C) with a purine nucleotide (G or A), or vice versa. The presence of this mutation can

available in the gene bank	•			-			-						-	
#Boerka Bali 1	ATT	ACA	AAG	CTG	CCT	GCC	CCT	TTC	CAG	GTT	CTA	GGA	AAT	[39]
#Boerka Bali 2														[39]
#Boerka Bali 3											Α			[39]
#Boerka Bali 4														[39]
#Boerka Bali 5														[39]
#Ovis_aries_(MH144568)														[39]
#Capra Attappady (KT315919)														[39]
#Capra Malabari (KT315918)														[39]
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#Boerka_Bali_1 #Boerka Bali 2														[78]
														[78]
#Boerka_Bali_3														[78]
#Boerka_Bali_4														[78]
#Boerka_Bali_5														[78]
<pre>#Ovis_aries_(MH144568)</pre>														[78]
#Capra_Attappady_(KT315919)														[78]
#Capra_Malabari_(KT315918)	• • •	•••	• • •	• • •	• • •	• • •	• • •		• • •	•••	• • •	• • •	• • •	[78]
#Boerka_Bali_1	-					-		TCT	-					[117]
#Boerka_Bali_2								• • •						[117]
<pre>#Boerka_Bali_3</pre>								• • •						[117]
#Boerka_Bali_4	• • •	•••		• • •	• • •	• • •	•••	• • •	• • •	• • •	• • •	• • •	• • •	[117]
#Boerka_Bali_5	•••	• • •	• • •	• • •	• • •	• • •	• • •	•••	•••	• • •	• • •	• • •	• • •	[117]
<pre>#Ovis_aries_(MH144568)</pre>														[117]
#Capra_Attappady_(KT315919)	ATC	A	GCG	C.G	TCT	.c.	AGT	CTA	GT.	.AC		AGT	CGT	[117]
#Capra Malabari (KT315918)														[117]
#Boerka Bali 1	TTT	GAG	GGT	TAA	AAT	CAT	AGA	GTA	TGC	TTG	AGA	TGG	т-с	[156]
#Boerka Bali 2													. – .	[156]
#Boerka Bali 3														[156]
#Boerka Bali 4														[156]
#Boerka Bali 5														[156]
#Ovis aries (MH144568)													. – .	[156]
#Capra Attappady (KT315919)														[156]
#Capra Malabari (KT315918)														[156]
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#Boerka Bali 2			-		-	-				-	-			[195]
#Boerka Bali 3														[195]
#Boerka Bali 4								•••						[195]
#Boerka Bali 5														[195]
														[195]
#Ovis_aries_(MH144568)	•••							· · ·						[195]
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#Capra_Malabari_(KT315918)	• • •	•••	•••	• • •	• • •	• • •	• • •	• • •	• • •	• • •	• • •	• • •	• • •	[195]
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#Boerka_Bali_1								CAT						[234]
#Boerka_Bali_2								• • •						[234]
#Boerka_Bali_3								•••						[234]
#Boerka_Bali_4								• • •						[234]
#Boerka_Bali_5								• • •						[234]
<pre>#Ovis_aries_(MH144568)</pre>								• • •						[234]
#Capra_Attappady_(KT315919)														[234]
<pre>#Capra_Malabari_(KT315918)</pre>	• • •	•••	• • •	• • •	• • •	• • •	• • •	• • •	• • •		• • •	Α	• • •	[234]
#Boerka_Bali_1	CCT	TTC	ATA	CGG	GTA	AGG	TA	[254]]					
#Boerka_Bali_2								[254]						
#Boerka_Bali_3								[254]						
#Boerka_Bali_4								[254]	-					
#Boerka_Bali_5	•••	• • •	• • •	• • •	• • •	• • •	••	[254]]					
#Ovis_aries_(MH144568)								[254]						
#Capra_Attappady_(KT315919)	.т.	.CA	TAC	G	TA.	G.T	G-	[254]]					
#Capra Malabari (KT315918)								[254]						

Table I: Alignment of the nucleotide sequence of the *IGF1* gene of Boerka goats raised in Bali with several *IGF1* gene nucleotides available in the gene bank

result in changes of codons which can have an impact on changes of the amino acids coded for. The existence of this mutation can also have an impact on the discovery of Boerka goat species with different *IGF1* gene alleles (Yakar et al. 2002; Putra et al. 2018). Further analysis of

the grouping of the nucleotide bases between the *IGF1* gene of Boerka goats and other goat breeds (Table 2).

Table 2 showed the base composition of the *IGF1* gene in Boerka goats was dominated by adenine base guanine (22.3%), and pyrimidine tyrosine (33.9%).

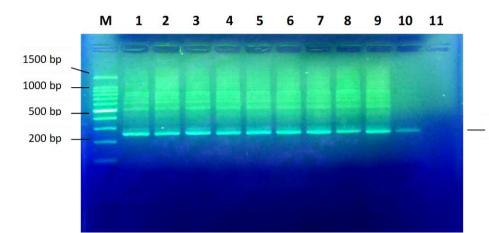


Fig. 1: PCR of the *IGF1* gene of Boerka goat with primers IGF677F and IGF897R on 1.5% agarose. M: 100 bp DNA Ladder marker (Promega), 1-10:
249 bp Boerka sample no. 1-10 and 11: Negative control.

These compositions were close to other goat breeds, namely *Ovis aries* (MT144568), New Zealand Romney sheep breed, Copra Attappady (KT315919) a goat breed which is known to be resistant to several diseases and extreme environments, and Capra Malabari (KT315918), a Malabari breed of goat that is bred as a meat and milkproducing type of goat in Kerala, India. Furthermore, genetic distance between them is shown in Table 3.

The data in Table 3 show the genetic distance between Boerka Bali 3 with Boerka Bali 1 and Boerka Bali 2 are 0.004 or 4/1000 nucleotides. A close similarity was also found between Boerka goats and Capra Malabari goats (KT315918) with a nucleotide difference of 8/1000 nucleotides against Boerka 1, Boerka 2, Boerka 4, and Boerka 5. Meanwhile, the nucleotide difference with Boerka 3 was 12/1000 nucleotides. According to Jorde and Wooding (2004), approximately 0.1-0.4% variation can be found if the individuals belong to single continent. Based on the results, it can be estimated that Boerka goats raised in Bali have a phenotypic appearance similar to the Capra Malabari goat (KT315918).

The phylogenetic tree of Boerka goats to other goat breeds as in Fig. 2. It can be interpreted from Fig. 2 that the Boerka Bali 1, Boerka Bali 2, Boerka Bali 3, Boerka Bali 4, and Boerka Bali 5 goats form one cluster together with *Ovis aries* (MH144568) and Capra Malabari (KT315918) with a bootstrap value of 99%, however, in different cluster from the Capra Attapaddy (KT315919). These results confirm that Boerka goats raised in Bali tend to have characteristics and appearance resembling *Ovis aries* and Capra malabari.

IGF1 is known to have an important role in various physiological processes. Its effects are predominant on growth, health, reproduction and lactation (McGuire et al. 1992; Rasouli et al. 2017; Norris and Carr 2021) as well as meat quality (Kader Esen and Esen 2023). *IGF1* stimulates postnatal body growth specifically regulate the synthesis of whole-body proteins, lipid methabolism, and uptake of glucose by peripheral tissues (Hadsell et al. 2002).

Several researchers have reported that IGF1 gene polymorphisms influence the growth and production traits in several livestock species. Single nucleotide polymorphisms (SNP) in the IGF1 promoter affect fat and carcass deposition in Charolais and Angus beef cattle (Islam et al. 2009), while the SNP polymorphisms in the IGF region-1 in goats are also known to influence growth traits (Zhang et al. 2008). Furthermore, Li et al. (2021) also

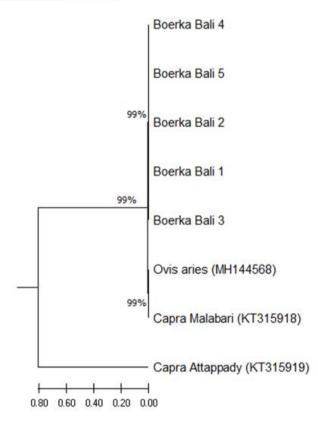


Fig. 2: Phylogenetic tree of Boerka goats based on the *IGF1* gene nucleotides (254 nt in size) against other goat breeds that was constructed based on the UPGMA algorithm (Saitou and Nei. 1987). Numbers on the phylogram branches indicate bootstrap values (%) with 500 replications.

 Table 2: Nucleotide composition of the IGF1 gene in Boerka goats compared to other goat breeds

Goats races	Nucle	Total			
	T(U)	С	А	G	_
Boerka Bali 1	33.9	23.9	22.3	19.9	251
Boerka Bali 2	33.9	23.9	22.3	19.9	251
Boerka Bali 3	33.9	23.5	22.7	19.9	251
Boerka Bali 4	33.9	23.9	22.3	19.9	251
Boerka Bali 5	33.9	23.9	22.3	19.9	251
Ovis arries (MH144568)	33.5	23.5	22.3	20.7	251
Capra Attappady (KT315919)	34.0	23.6	22.4	20.0	250
Capra Malabari (KT315918)	33.5	23.9	22.3	20.3	251

found that polymorphisms of the *IGF1* gene in goats in the exon 3 region could potentially be used as a marker for growth and carcass traits.

Table 3: Genetic distance of Boerka goats and other goat breeds based on the IGF1 gene

	Boerka	Boerka	Boerka	Boerka	Boerka	Ovis arie	es Capra Attappady	Capra Malabari
	Bali 1	Bali 2	Bali 3	Bali 4	Bali 5	(MH144568)	(KT315919)	(KT315918)
Boerka Bali 1								
Boerka Bali 2	0.000							
Boerka Bali 3	0.004	0.004						
Boerka Bali 4	0.000	0.000	0.004					
Boerka Bali 5	0.000	0.000	0.004	0.000				
Ovis aries (MH144568)	0.012	0.012	0.016	0.012	0.012			
Capra Attappady (KT315919)) 1.627	1.627	1.614	1.627	1.627	1.581		
Capra Malabari (KT315918)	0.008	0.008	0.012	0.008	0.008	0.004	1.594	

Polymorphisms of *IGF1* have been investigated in dairy sheep (Sebastiano et al. 2020). The study showed that *IGF1* is a potential candidate gene for reproduction and milk yield. In the study of the Sarda breed, three nucleotide variations of the IGF-I gene in the 5' UTR region and Exon 3 were found, and three SNP investigated are involved in regulating the milk production and reproductive activity of the Sarda sheep breed (Sebastiano et al. 2020). Moreover, polymorphisms of the *IGF1* gene were found to be associated with higher body weight of Munjal sheep, and can be used in selection criteria for improving the performance (Kumar et al. 2023).

Based on the results of IGF1 gene analysis which found high similarity of the DNA composition and placed Boerka goats in one cluster with Ovis aries (MH144568) and Capra Malabari (KT315918) that indicated among them have close phenotype. Ovis aries is known to have a large and complex stomach that can digest highly fibrous foods that can not be digested by many other animals. Its moderate nutritional requirements contribute to its economically significant species. They have been a source of meat, milk, wool and hides and can be maintained in many environments at relatively low cost (Hecker 1983; Ben Sassi-Zaidy et al. 2022). The phylogenetic tree also showed that the Boerka goats raised in Bali have close similarities to Malabari goats bred in the Malabar district in Kerala, India. The goats are bred mostly for meat, but also produce milk, and the Malabari breed of goat is also famous for its low-fat meat and high prolificacy. This goat is well adapted to the hot and humid conditions of Kerala state (Verma et al. 2009). In contrast, Attappady black sheep in a different cluster are found exclusively in Attappady, a remote hilly area in Kerala, India. This goat has black bronze eyes. This goat is slightly larger than the Boerka goat, i.e., body length (67±0.8cm) and body weight (31±0.4kg) compared those reported by Suyasa et al. (2023). They found the body length and body weight of Boerka goats to be 68.85+5.15cm and 29.04+4.51kg, respectively, but it is still smaller than the Etawah crossbred goat (Stephen et al. 2011).

The correlation between the growth characteristics and *IGF1* concentrations has been studied by Pehlivan (2019). The study showed climatic factors such as temperature, photoperiod, and the index of temperature–humidity have a significant effect on the *IGF1* concentrations in the goat kids. The photoperiod and the environmental temperature have significant effects on the increase of the *IGF1* release. A similar findings have been found a previous study (Sarko et al. 1994) who reported that *IGF1* concentrations are significantly affected by environmental factors in farm animals. The close study on ruminants also stated that seasonal changes such as photoperiod are mainly driven by

change in *IGF1* concentrations (Dahl et al. 1997). Hernandez et al. (2016) also stated the photoperiod has a significant effect on the *IGF1* concentrations of the goats.

The use of IGF-1, as one of the genes involved in controlling growth traits to complement the information used in the MAS-based sheep selection program (Marker Assisted Selection) has been studied by several researchers. Polymorphism in the 5'-flanking region in the IGF1 of Polish Moreno sheep showed it not only affected growth and body size but also affected carcass and meat quality traits (Grochowska et al. 2017). Another study in Santa Ines sheep, showed SNPs in IGF1 intron 1 were found to be associated with many carcass traits including rump girth, internal carcass length, neck weight, and rib yield (Meira et al. 2019). The study in 848 New Zealand Romney lambs using PCR-single strand conformation polymorphism (SSCP) analyses for nucleotide sequence variation in three regions of ovine IGF1 (part of the 5' flanking region showed that polymorphism in exon 3 of ovine IGF1 has potential for use as a gene-marker for some carcass and growth traits (Li et al. 2021). Furthermore, the association between IGF1 and IGF-1R genetic polymorphisms and growth traits in Hulun Buir sheep has been studied by Ning Ding et al. (2022). Their study identified three and 10 single nucleotide polymorphisms (SNPs) in exons of IGF1 and IGF-1R in Hulun Buir sheep were significantly (P<0.05) associated with four growth traits so that they can be used to as marker-assisted selection (MAS). On the other hand, the study by Malewa and Awaludin (2022) has not found a significant correlation between phenotypic performance of body weight and bone size with the IGF1 polymorphisms of Palu sheep. Based on the results of several studies it can be mentioned the importance of the IGF1 study to investigate the genetic distance among animals and also to identify the correlation of genetic and phenotype performance of the animal, although several studies have not yet found an insignificant effect.

Conclusion

Boerka goats raised in Bali genetically share a clade with *Ovis aries* and *Capra malabari* with a bootstrap value is 99% as a type of meat and milk goats. These results indicated that Boerka goats tend to have characteristics and appearance resembling *Ovis aries* and *Capra malabari* goats.

Author's Contribution

I Wayan Suardana: Conceptualized and designed the study and critically revised the manuscript; I Nyoman Suyasa collected data resources and project administration. Both authors have read, reviewed, and approved the final manuscript.

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Competing Interests

The authors declare that do no competing interests according to this manuscript.

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