Genome-wide characterization of runs of homozygosity and estimation of genomic inbreeding in Ugandan goat breeds

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Summary

Domestication and selection in livestock species tend to leave unique genomic imprints in the genome. Under intense selection pressure, these genomic regions show reduction in genetic diversity (runs of homozygosity, ROH). Analysis of ROH provide an informative indicator for inbreeding levels. Using genome-wide SNP data, we analysed six local goat breeds from Uganda to compare the distribution of ROH across different length categories within the breeds with a cut-off threshold of 2 Mb. Genomic inbreeding was calculated from the ≥2 Mb ROH for each individual and averaged across the breeds. We further investigated the variation in inbreeding at a higher ROH threshold of 4 Mb. A total of 1,437 ROH segments ≥ 2 Mb were detected with differing frequency and length distribution across the breeds. The Boer breed show the highest overall frequency. Short ROH were generally more frequent than longer (> 20 Mb). High ROH coverage within the short category may indicate a relatively high contribution of more distant inbreeding in the breeds. These findings are useful for providing insights into the demographic history and designing strategies for sustainable breeding programs and conservation strategies for the breeds.

Keywords: Demographic history, breeding programs, inbreeding, local goat breeds

Introduction

Modern livestock species are a result of several generations of natural and artificial selection. Selection may favour utilization of certain individuals in the population leading to high levels of homozygosity in the genome, and increased inbreeding. Inbreeding due to genetic forces such as intense selection and genetic drift is particularly pronounced in situations of small effective population size leading to unequal contribution of individuals to the gene pool of the population. Inbreeding may have detrimental effects on performance and fitness of animal populations, a process commonly referred to as inbreeding depression (Bjelland *et al.,* 2013). With particular reference to livestock, inbreeding is accompanied by decrease in genetic diversity, increase in (expression of) deleterious alleles and reduced performance of production and fertility consequently impacting on profitability and sustainability of production (Bjelland *et al.,* 2013).

The extent of inbreeding in livestock can be indicated by the presence of stretches of homozygous segments of DNA sequence referred to as runs of homozygosity (ROH), as these ROH are caused by parents transmitting identical haplotypes to their offspring (McQuillan *et al.,* 2008). The ROH distribution across the genome can be a potential indicator for recent or ancient incidence of selective pressure on specific genomic regions

(Purfield *et al.,* 2012; Zhang *et al.,* 2015). Recombination breaks up chromosomal segments over generations. The presence of short segments across the genome will therefore capture information on more distant inbreeding (i.e. inbreeding on ancestors from many generations ago) and long segments are mostly due to recent inbreeding This information has recently been utilized in characterizing cattle, sheep and goat breeds elsewhere, but has rarely been undertaken for Ugandan goat breeds. Therefore, the objective of the study was to characterize ROH and estimate the extent of genomic inbreeding in Ugandan goat breeds using genomic markers covering the whole genome.

Material and methods

Sampling and genotype data

Samples from six goat breeds, Mubende (n = 29), Kigezi (n = 29), Small East African (n = 29), Karamojong (n = 15) and Sebei (n = 29), and exotic Boer (n = 13), were genotyped with the Illumina GoatSNP50 BeadChip (Tosser-Klopp *et al.,* 2014). Genotyping quality control (QC) procedures were performed using PLINK v1.90 (Chang *et al.,* 2015) to remove SNPs located on non-autosomal regions of the genome, with unknown or duplicated position, call rate lower than 95%, minor allele frequency (MAF) lower than 0.05 and departure from Hardy–Weinberg equilibrium test (P- value = 0.001). After QC, 46,105 SNPs and 144 animals were used for further analyses.

Identification of ROH

Runs of homozygosity were characterized and defined in each of the six goat populations using an in-house script. The ROH were called if 20 or more consecutive SNPs were homozygous, with a minimum physical length of 2 Mb and a maximum gap between consecutive SNPs of 500 kb. Within a ROH, 2 missing genotypes and no heterozygous calls were allowed. The ROH were estimated in each individual separately and then categorised into ten length categories of 2 Mb intervals (e.g. 2 – 4 Mb), with > 20 Mb as the last category. For each length category, the mean ROH genome coverage per breed was obtained by summing up all the ROH in individual animals and dividing by the total number of animals per breed.

Genomic inbreeding based on ROH

A genomic inbreeding coefficient based on ROH (F_{ROH}) was calculated as the proportion of the total genome length covered by ROH. The F_{ROH} was calculated for each individual for fixed ROH length of ≥ 2 Mb and ≥ 4 Mb.

Results and discussion

Runs of Homozygosity

A total of 1,437 ROH segments ≥ 2 Mb were detected across all the six breeds. The overall frequency of ROHs and their length-distribution differed across the six breeds. They were generally more frequent in Boer (a commercial breed for meat production) than in the Ugandan indigenous goat breeds (Table 1). Within the latter breeds, Sebei had the lowest ROH frequency. In fact, approximately 48% and 86% of the Sebei individuals showed no

ROH ≥2 Mb or ≥4 Mb, respectively. Boer has undergone intensive selection since its development in South Africa (Casey & Van Niekerk, 1988). The Ugandan indigenous goat breeds have hardly undergone breed specific artificial selection and are highly outbred, which might explain the observed differences in ROH frequencies.

Table 1. Distribution of ROH segments at different length categories across six Ugandan goat breeds

Length category (Mb)	BOE (n = 13)	KAR (n = 15)	KIG (n = 29)	SEB (n = 29)	SEA (n = 29)	MUB (n = 29)
$ROH_{(2-4)}$	464	21	145	25	71	66
$ROH_{(4-6)}$	181	8	22	6	14	17
$ROH_{(6-8)}$	89	4	12	5	9	7
$ROH_{(8-10)}$	51	4	8	2	2	5
$ROH_{(10-12)}$	32	10	7	0	3	5
$ROH_{(12-14)}$	16	4	3	3	4	3
$ROH_{(14-16)}$	7	4	1	1	4	3
$ROH_{(16-18)}$	8	3	1	2	5	5
$ROH_{(18-20)}$	5	2	2	3	1	6
$ROH_{(>20)}$	8	13	3	8	8	6

Goat breeds assessed; BOE= Boer, KAR=Karamojong, KIG=Kigezi, SEB=Sebei, SEA= Small East African and MUB= Mubende.

The mean sum of ROH segment coverage was generally higher for short ROHs than for long ROHs (Figure 1). For example, about 85% of the Boer ROH segment coverage in this study was within the ROH category 2 Mb – 8 Mb. An exception was found for Karamojong, which showed a higher average sum of ROH coverage > 20 Mb. The distribution of ROH coverage reported here is in agreement with other studies in goats (Brito *et al.,* 2017), sheep (Purfield *et al.,* 2017) and cattle (Ferenčaković *et al.*, 2013; Mastrangelo *et al.,* 2016) in which long ROH segments were found less frequently compared to shorter ones. The highest mean ROH coverage within the short ROH category was found in Boer, while Sebei had the lowest of mean ROH coverage. This may be due to differences in selection events in the more recent or ancestral populations. The higher proportion of ROH segments within the short ROH categories indicates a relatively larger contribution of distant inbreeding, whereas the higher coverage of long ROH observed in Karamojong suggests a larger effect of more recent inbreeding.

Figure 1 Distribution of mean sum of ROH coverage per length category averaged per breed across six goat breeds in Uganda (Boer, Karamojong, Kigezi, Mubende, Small East African and Sebei)

Genomic inbreeding

Genomic inbreeding coefficients were substantially higher in Boer than in the indigenous Ugandan goat breeds, both for F_{ROH}(2Mb) as for F_{ROH}(4Mb) (Table 2). Brito et al. (2017), using the 50K reported F_{ROH} for Canadian and Australian Boer of 0.057 and 0.047, respectively.

Table 2: Mean genomic inbreeding (F_{ROH}) at two different ROH thresholds across six goat populations

		$F_{ROH \geq 4Mb}$			$F_{ROH \geq 2Mb}$		
Breed	n	Mean	Range	N_0	Mean	Range	N_0
Boer	13	0.0969	0.044 – 0.154	0	0.1387	0.062-0.202	0
Karamojong	15	0.0230	0 – 0.136	8	0.0244	0 – 0.137	2
Kigezi	29	0.0075	0 – 0.052	11	0.0127	0 – 0.055	1
Mubende	29	0.0095	0 – 0.092	18	0.0121	0 – 0.162	5
Small East African	29	0.0091	0 – 0.100	17	0.0119	0 – 0.098	2
Sebei	29	0.0071	0 – 0.157	25	0.0080	0 – 0.106	14

N_0 Number of individuals from the samples for which no ROH were detected, $F_{ROH \geq 4Mb}$ = Genomic inbreeding at ROH threshold of 4Mb, $F_{ROH \geq 2Mb}$ = Genomic inbreeding at ROH threshold of 2Mb.

Conclusion

Genomic inbreeding in the Ugandan indigenous goat breeds is generally lower compared to Boer goats at the ROH threshold considered in this study. Our findings indicate the need to continue monitoring rate of inbreeding and implement strategies to minimize inbreeding in breeding programs emphasizing the use of the Boer breed.

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