Functional longevity is heritable and controlled by a major gene in French dairy goats

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Summary

Longevity is an indirect global trait to quantify productive lifespan of livestock, and for increasing durability and profitability of farms. Functional longevity was analyzed in 1,137,793 Saanen and Alpine goats by incorporating first lactation milk yield in the statistical model. Heritabilities were estimated using linear mixed models and Wombat software. Genetic correlations with production traits, SCC and udder type traits were estimated in a subset of 341,982 goats. Genetic correlations of functional longevity with milk production were generally low (rg from -0.06 to 0.28). Genetic correlations of functional longevity were negative with LSCS (rg from -0.29 to -0.35) and positive with udder floor position and rear udder attachment (rg from 0.17 to 0.29). Such favourable genetic associations suggest that good udder health and udder shape significantly contributes to higher functional longevity in goat. Daughter yield deviations for functional longevity were computed for 18,945 AI bucks. DYD showed no significant trend over the past decades, suggesting that genetic merit for functional longevity has not deteriorated. Further, a genome wide association study for functional longevity was conducted on 639 Saanen and Alpine bucks genotyped with the Illumina GoatSNP50 BeadChip. A highly significant (p-value min = 1.94e-09) QTL was found on chromosome 19 (26.19 - 28.87 Mb) in the Saanen breed. Altogether, results prepare a possible inclusion of longevity in the French goat breeding programs. Information on longevity-associated genomic regions could be used to find causal genes and mechanism underlying the trait and utilized to improve the reliability of genomic prediction.

Keywords: functional longevity, genetic parameters, genome wide association, goats

Introduction

Longevity is an indirect global trait to quantify productive lifespan of livestock, and for increasing durability and profitability of farms. In dairy ruminants, longevity definitions include: (i) true longevity (all culling reasons, including milk productivity); and (ii) functional longevity (all culling reasons, except milk productivity) (Sasaki, 2013). Functional longevity (corrected for production level) reflects the animals’ accumulated ability to overcome health and nutritional challenges. It is an indirect global approach to quantify adaptive capacity to various production environments.

Genetic basis of functional longevity is well documented in cattle (Ducroq and Sölkner, 1994; Sasaki, 2013; Castañeda-Bustos et al., 2017). Genetic variation among individuals exists (heritability around 10%) so that selection can improve this trait which has been eroded in the past decades. The development of high-density single nucleotide polymorphism (SNP) arrays and their application in genome-wide association studies can facilitate the identification of regions that control such complex traits. However, the main physiological mechanisms and genes underlying functional longevity are still largely
unknown.

The objective of this study was to assess the possibility for improving functional longevity in dairy goats. We first fitted a definition and a model for functional longevity. We then estimated heritability of the trait and genetic correlation with other traits that are already included in the breeding objective. The availability of data from bucks genotyped with the Illumina GoatSNP50 BeadChip allowed us to further conduct the first genome wide association study for functional longevity in this species.

Material and methods

Animals

Data came from a total of 520,972 Saanen goats and 616,821 Alpine goats. Goats were born between 1991 and 2011 in 3,545 flocks and were part of the official milk recording scheme (Dataset1). Because of computational challenges, a subset of goats kidding from 2000 to 2011 was selected to estimate genetic correlations of functional longevity with milk production and udder type traits (Dataset2). Dataset2 included 135,197 goats from 3747 sires in the Saanen breed and 206,785 goats from 4871 sires in the Alpine breed.

Phenotypes

Length of productive life (LPL) was computed in Dataset1 as the time interval (in days) between first kidding and the last milk recording registered in the national data base. All females had the opportunity to have a LPL at least equal to 6 years.

Milk production traits and udder type traits were computed in Dataset2. Milk production traits included first lactation average (in 250 days) for milk yield (MY), fat and protein yields (FY and PY), fat and protein contents (FC and PC) and somatic cell score (LSCS) as described in Rupp et al. (2011). The following five udder type traits were also considered: fore udder (FU), udder profile (UP), udder floor position (UFP), rear udder attachment (RUA), and teat orientation (TO). The definition of the traits is presented in Manfredi et al. (2001). All type traits were recorded once by official classifiers from the breeders’ association Capgènes (Mignaloux Beauvoir, France). Only the goats sired by AI bucks (39%) were recorded for udder type traits, i.e. 49,007 Saanen goats and 84,454 Alpine goats.

Genetic parameter estimation and computation of daughter yield deviations

Heritabilities and genetic correlations were estimated by univariate and multivariate REML, using the software WOMBAT (Meyer, 2007). Analyses were run separately for Alpine and Saanen breeds. Heritabilities for LPL were estimated using single trait linear mixed models in dataset1. The model used for dataset1 and dataset2 included the fixed effects of flock by birth year combination, age at first kidding, month at first kidding, and 250 day milk production in first lactation (10 levels within flock by year combination). The milk production in first lactation was added to the model for LPL, in order to conduct a genetic study for functional longevity that is independent from voluntary culling decisions based on milk production levels. The random elements were the random animal additive genetic effect and the random residual effect. Five generations of ancestors were traced back and the total number of animals in the relationship matrix was 850,118 and 735,449 in Alpine and Saanen
breeds, respectively. Genetic correlations with LPL were computed from two traits runs in Dataset2 with multitrait models. For MY, FY, PY, FC, PC and LSCS, the fixed effects in the model were: flock, age and month at kidding, defined within year of birth. For FU, UP, UFP, RUA, and TO the fixed effects in the model were: flock, age and lactation stage, defined within year of scoring.

Yield deviations for LPL were then estimated in Dataset1 using “Best Linear Unbiased Predictions” (BLUP) based on phenotypic, pedigree information and variance component estimates. For each sire buck with at least 10 daughters, one single daughter yield deviation (DYD) was computed as the mean of all its daughter’s yield deviations. Accordingly DYDs for LPL was computed for a total of 10,158 and 8,787 bucks.

Genotyping and Genome wide association study (GWAS)

A total of 298 Saanen and 341 Alpine bucks with DYD for LPL were genotyped with the Illumina GoatSNP50 BeadChip (53,347 SNPs). Quality control of genotypes and GWAS were performed separately per breed. After quality control 46,778 SNPs (Saanen) and 46,780 SNPs (Alpine) distributed on goat autosomes CHI 1 to CHI 29 were analyzed. GWAS were performed using the univariate mixed model approach implemented in the Genome-wide Efficient Mixed Model Association (GEMMA) software (Zhou & Stephens, 2012). A Bonferroni correction of α = 5% was applied to Wald test p-values (significance threshold = α/number of SNP). SNPs with a p-value < 1.07e-06 were considered to be significantly associated at the genome level.

Results and discussion

Observed longevity is decreasing over the past 20 years

Average LPL over the three past decades was 967 days (± 695) in Saanen and 1007 days (± 710) in Alpine goats. Accordingly, age at culling was 3.8 and 3.9 years in Saanen and Alpine breeds, respectively. Noteworthy, LPL showed regular decrease from birth year 1991 to birth year 2010 (Add.data1). The decrease was similar in both breeds and averaged 320 days in ten years. This trend was related to an increase in the voluntary replacement rate, which has increased from 20% in the nineties to about 30% nowadays. Daughter yield deviations for LPL however did not decrease, suggesting that genetic merit for functional longevity has not deteriorated.

Functional longevity is heritable and genetically correlated to udder type and somatic cell score

Heritability of LPL was equal to 0.07 (±0.003) in Saanen and 0.08 (±0.002) in Alpine. Estimates were in the range of values for similar traits using linear models in cattle (review by Sasaki, 2013) and goats (h²=0.14) (Castañeda-Bustos et al., 2017).

Genetic correlations with fat and protein yields and contents were close to zero (Add.data2). Genetic correlations between LPL and milk yield, however, were slightly positive (rg=0.16 ± 0.05 in Saanen and rg=0.28 ± 0.04 in Alpine). This result suggested that although LPL was corrected for milk yield, higher functional longevity is partly genetically associated with higher production in the current model.

Genetic correlations of LPL were negative with LSCS (rg from -0.29 to -0.35) and
positive with RUA and UFP (rg from 0.17 to 0.29). Such favourable genetic association of LPL with udder type or LSCS was consistently reported in cattle (Sasaki 2013), and in goats for udder type (Castañeda-Bustos et al., 2017), suggesting that good udder health and udder shape significantly contributes to higher functional longevity in goat.

A highly significant QTL for functional longevity in the Saanen breed

GWAS identified no significant association with LPL in the Alpine breed (Add.data3). In Saanen, one region of chromosome 19 was highly significant with 5 SNPs above the 5% genome wise threshold spanning a region from 26.19 to 28.87 Mb (Add.data4). The SNP snp10603-scaffold1377-32250 was the most significant with a p-value equal to 1.94e-09 (-log10(p) = 8.71). The region exhibited 155 candidate genes. The region was previously found associated with milk production (Martin et al., 2017) and udder type traits in the same population (Martin, personal communication). This result suggests one single pleiotropic QTL or closely linked QTLs. The region did not match any QTL reported for longevity in cattle (Zhang et al., 2016).

Conclusion

LPL is a heritable trait in goats and can be used as a proxy for improving functional longevity in this species. LPL is genetically correlated to LSCS, RUA and UFP which can be considered as predictor of functional longevity. The highly significant QTL for functional longevity found in the Saanen breed can provide information to improve efficiency of selection and better knowledge about genes and mechanisms underlying this complex trait.

List of References

Add data1. Length of productive life (LPL) in Saanen and Alpine dairy goats according to birth year.

Add data2. Basic statistics for eleven milk production and udder type traits, heritabilities and genetic correlation with LPL in Saanen and alpine dairy goats. Milk production traits and LSCS were measured in 135,197 Saanen and 206,785 Alpine goats. Udder type traits were measured in 49,007 Saanen and 84,454 Alpine goats.

<table>
<thead>
<tr>
<th>Trait</th>
<th>Mean</th>
<th>Rg with LPL</th>
<th>Saanen</th>
<th>Alpine</th>
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<tbody>
<tr>
<td></td>
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<tr>
<td>MY, kg</td>
<td>903 ± 242</td>
<td>0.16 ± 0.05</td>
<td>0.28 ± 0.04</td>
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<tr>
<td>PY, kg</td>
<td>27.7 ± 7.4</td>
<td>0.02 ± 0.05</td>
<td>0.14 ± 0.04</td>
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<tr>
<td>FY, kg</td>
<td>31.9 ± 9.6</td>
<td>-0.06 ± 0.05</td>
<td>0.13 ± 0.04</td>
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<tr>
<td>PC, g/kg</td>
<td>30.7 ± 2.3</td>
<td>0.01 ± 0.05</td>
<td>0.02 ± 0.04</td>
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<tr>
<td>FC, g/kg</td>
<td>35.4 ± 4.9</td>
<td>0.03 ± 0.05</td>
<td>0.10 ± 0.04</td>
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<tr>
<td>LSCS</td>
<td>5.4 ± 1.3</td>
<td>-0.29 ± 0.05</td>
<td>-0.35 ± 0.04</td>
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<tr>
<td>UP</td>
<td>6.2 ± 1.3</td>
<td>-0.03 ± 0.05</td>
<td>0.02 ± 0.04</td>
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<td></td>
<td>FU</td>
<td>TO</td>
<td>RUA</td>
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<tr>
<td>Trait definition : 250-d milk yield (MY), 250-d fat and protein yields (FY and PY), fat and protein contents (FC and PC) and somatic cell score (LSCS), fore udder (FU), udder profile (UP), udder floor position (UFP), rear udder attachment (RUA), teat orientation (TO).</td>
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</table>

### Add.data3.
Manhattan plot of genome-wide association analysis results of length of productive life (LPL) in Alpine goats

### Add.data4.
Manhattan plot of genome-wide association analysis results of length of productive life (LPL) in Saanen goats