Genome-wide Association Mapping for Type and Mammary Health Traits in French Dairy Goats

P. Martin¹, I. Palhière¹, C. Maroteau¹, V. Clément¹, G. Tosser-Klopp¹ & R. Rupp¹

¹ GenPhySE, Université de Toulouse, INRA, INPT, ENV'T, Castanet Tolosan, France
pamarti05@uoguelph.ca (Corresponding Author)

Summary

Type traits and mammary health are important traits for dairy ruminant breeding. They govern animal health, milking ability and longevity as well as the economic sustainability of farms. However, little is known about the genomic regions controlling these traits in goat. We report here a genome-wide association study in dairy goats for eleven type traits, and SCC, as a proxy for mastitis resistance. The analysis was implemented using a daughter design composed of 1941 Alpine and Saanen goats sired by 20 AI bucks and genotyped with the goatSNP50 chip. Both linkage analyses (LA) and linkage disequilibrium (LD) using interval mapping were performed and the two breeds were analysed together and separately.

A large number of QTL regions was highlighted, suggesting that the genomic control of type and SCC traits is highly polygenic in goats. Moreover, the regions found were different between Alpine and Saanen, revealing a breed-specific control. The Capra hircus autosome (CHI) 19 appeared to be especially enriched in SNPs associated with type and SCC, with two highly significant regions in the Saanen breed. The first region is located between 33 and 42 Mb on CHI 19 and was significantly associated with SCC. This interval contains or is in close proximity to candidate genes that could be involved in response to intra-mammary infections (RARA, STAT3, STAT5a and STAT5b). The second region, located between 24.5 and 27 Mb on CHI 19 was associated with udder type traits (udder floor position and rear udder attachment) in the same interval that had been associated previously with milk production traits. This region and its potential pleiotropic effects is currently under investigation. Altogether, these results will be helpful for goat selection in the future. It indicates that a within-breed genomic selection should be favoured for those traits in French goat and open the way to the identification of causal mutations.

Keywords: type traits, somatic cell count, genome wide association, goat

Introduction

Type traits and mammary health are important traits to dairy ruminant breeding. Udder morphology impacts the duration of the productive life of the animals by reducing premature culling due to morphological defects (Clément et al., 2006). Moreover, the milk somatic cell score (SCS), an indirect predictor of udder health status (Rupp and Foucras, 2010), is also a means of reducing clinical and subclinical mastitis and has been highlighted to improve both animal health and milk quality. Accordingly, the French goat breeding program includes milk production and composition, but also five udder type traits and SCS in its selection objective. However, very little is known about the loci controlling type traits and SCS in goat. The recent development of a high-density single nucleotide polymorphism (SNP) array (Tosser-Klopp et al., 2014) has opened up new fields of investigation to better understand and select
for traits of interest in this species.

In this paper, we report a genome scan for twelve traits, including ten udder type traits, SCC and stature in Saanen and Alpine dairy breeds.

**Material and methods**

**Animals and genotyping**

The data was provided from a total of 2,209 French dairy goats sampled in 2010 as part of the national "Genomcap" and the EU "3SR" (www.3srbreeding.eu) projects already described in Martin et al. (2017). The 2,209 animals were distributed in 20 half-sib families sired by 9 Saanen and 11 Alpine animal insemination (AI) bucks. They were genotyped using the Illumina GoatSNP50 BeadChip (53,347 SNPs). Data was cleaned using an in-house pipeline as in Martin et al. (2017). After edits, 1985 animals remained and a total of 44,612 SNPs distributed on goat autosomes CHI 1 to CHI 29 were included for further analyses.

**Phenotypic measurements**

The following 11 type traits were considered: fore udder (FU), udder profile (UP), udder floor position (UFP), rear udder (RU), rear udder attachment (RUA), teat length (TL), teat form (TF), teat angle (TA), teat orientation (TO), chest depth (CD), and foot orientation (FO). The definition of the traits is presented in Manfredi et al. (2001). All type traits were recorded once, during the first or possibly second lactation of the animals, by official classifiers from the breeders’ association Capgènes (Mignaloux Beauvoir, France).

The LSCS was computed as described by Rupp et al. (2011). The monthly test-day SCC were transformed to somatic cell scores (SCS) by logarithmic transformation to achieve a normal distribution. A lactation SCS was then computed as the weighted arithmetic mean of the test-day SCS adjusted for days in milk.

For genome-wide association testing, yield deviations (YDs) for all traits were used as provided by the official French national genetic evaluation. The YDs for each lactation (only the first 3 lactations were considered) were averaged by animal. A total of 1,941 phenotyped and genotyped animals were used for QTL mapping.

**Association mapping**

QTLs associated with the 11 type traits and LSCS were mapped separately by breed as well as combined in a joint analysis. Both linkage analyses (LA) and linkage disequilibrium (LD) using interval mapping were applied using the QTLMap software ((Elsen et al., 1999); http://dga7.jouy.inra.fr/qtlmap/). For LA, interval mapping was performed with the likelihood ratio test (LRT) using within-sire linear regression (Knott et al., 1996). The QTL effect (average substitution effect) was expressed in phenotypic deviation units (SD) for the trait. LD was based on a regression analysis of the phenotypes against the founder haplotypes (Legarra and Fernando, 2009). Both LA and LD analyses provided a test for each genomic position (here every 0.1 Mb, i.e. 24,015 tests over the genome) using the surrounding SNP information. Chromosome-wide significance levels were calculated with QTLMap, using the current family structure and the milk yield trait from Martin et al. (2017). The 5% genome-wide thresholds were obtained by applying the Bonferroni correction.
Results and discussion

A very large number of QTLs

From the LA, 37 QTLs were detected at the 1% chromosome-wide threshold and among them, seven hits in four regions of chromosomes CHI 1, 6, 8 and 19 exceeded the 5% genome-wide threshold. From the association mapping, a total of 222 hits (454 SNPs) exceeded the 5% genome-wide threshold. These hits were scattered across the genome, with enrichment on CHI 6, 8, 14 and 19 and with a range of 12 to 32 hits per trait.

Two Goat Breeds with different Genetic Control

When the two breeds were compared, more hits were detected in Saanen (n=73, total number of SNPs=182) than in Alpine (n=55, total number of SNPs=116) goats, even though the design included more Alpine families and goats. Among those association results, only one hit was shared by the two breeds when examined separately (TF at 73.2 and 77 Mb on CHI 14). The significant positions detected for the two breeds analysed jointly were either new regions (not found in the single breed analysis) or regions detected in one of the two breeds taken separately. In most cases, the results from the two breeds combined in a joint analysis did not strengthen the single breed results. These results suggest that the genes responsible for those traits, or allele frequencies, truly differ between the 2 breeds.

Four regions of particular interest

Four regions were especially significant as presented figure 1. First, a CHI 19 region that was associated with udder type in the Saanen breed (UFP using LA, 5% CI: 24.1-29.7 Mb, and both UFP and RUA using LD, 5% CI: 24.4-26.4 Mb). The QTLs explained 5% of variance for each of the two traits. The region was previously found associated with milk production traits for both breeds (Martin et al., 2017). This suggests one single pleiotropic QTL or two closely linked QTLs.

Another CHI 19 region was also particularly interesting for its strong association with LCSC in the Saanen breed (LA 5% CI: 40.8-42.1 and LD 5% CI: 35.0-35.2). This QTL explained 4% of the trait variance and is located near four genes potentially involved in response to intra-mammary infections (RARA, STAT3, STAT5a and STAT5b).

Finally, one region on CHI 6 (5% CI: 45.8-46.0 Mb) and one region of CHI 8 (5% CI: 80.7-81.1 Mb) were associated with CD in the Alpine breed using LD. The QTLs explained 6 and 3% of variance for the trait, respectively.

Figure 1. Manhattan plots of likelihood ratio tests on chromosomes 1 to 29 for three type traits: (a) udder floor position (UFP) in Saanen, (b) rear udder attachment (RUA) in Saanen,
Conclusion

The numerous regions identified in this study improved our knowledge of the genomic control of type and udder health traits in dairy goat. These results will be helpful for French breeding programmes in the future and could lead to the identification of causal mutations. The breed specific genomic determinism indicates that a within-breed selection should be favoured for those traits. Fine mapping is in progress for several QTL regions. In particular, a CHI 19 region is under further investigation in order to determine if it is a single pleiotropic QTL or two different, but very close, QTLs. QTLs, haplotypes or causal mutation will be valuable information to improve efficiency of genomic selection.

List of References


