



Detection of quantitative trait loci for resistance to gastrointestinal nematode infections in Creole goats

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Summary

This study aimed to identify regions of the genome affecting resistance to gastrointestinal nematodes in a Creole goat population naturally exposed to a mixed nematode infection (*Haemonchus contortus*, *Trichostrongylus colubriformis* and *Oesophagostomum columbianum*) by grazing on irrigated pasture. A genome-wide quantitative trait loci (QTL) scan was performed on 383 offspring from 12 half-sib families. A total of 101 microsatellite markers were genotyped. Traits analysed were faecal egg count (FEC), packed cell volume (PCV), eosinophil count and bodyweight (BW) at 7 and 11 months of age. Levels of activity of immunoglobulin A (IgA) and activity of immunoglobulin E (IgE) anti-*Haemonchus contortus* L3 crude extracts and adult excretion/secretion products (ESPs) were also analysed. Using interval mapping, this study identified 13 QTL for parasite resistance. Two QTL linked with FEC were found on chromosomes 22 and 26. Three QTL were detected on chromosomes 7, 8 and 14 for eosinophil counts. Three QTL linked with PCV were identified on chromosomes 5, 9 and 21. A QTL for BW at 7 months of age was found on chromosome 6. Lastly, two QTL detected on chromosomes 3 and 10 were associated with IgE anti-L3, and IgE anti-ESP was linked with two QTL on chromosomes 1 and 26. This study is the first to have identified regions of the genome linked with nematode resistance in a goat population using a genome scan. These results provide useful tools for the understanding of parasite resistance in small ruminants.

Keywords antibodies, faecal egg count, gastrointestinal nematode resistance, goat quantitative trait loci detection.

Introduction

Gastrointestinal parasite infections remain one of the major constraints to small ruminant production in temperate and tropical climates (Perry & Randolph 1999). Anthelmintics have been widely used in the past for parasite control despite the presence of parasite strains showing some degree of resistance to the molecules used

(Sangster 1999). In terms of alternative strategies, the development of effective vaccines and the selection of resistant animals are the most promising complementary control methods (Eady *et al.* 2003).

Selection for increased resistance exploits the genetic variability in resistance observed in most commercial sheep breeds and in some goat breeds (Baker & Gray 2004). One approach is to select resistant animals using phenotypic traits such as the faecal egg count (FEC), which is an indirect measure of resistance. Selection for phenotypic traits has been successfully used in Australia and New Zealand (Karlsson *et al.* 1991; Kemper *et al.* 2010); however, it is costly and time-consuming as it requires animals to be challenged with parasites. The emergence of new technologies in molecular biology has

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allowed a second approach consisting of combining phenotypic and genotypic information for selection. For example, quantitative trait loci (QTL) could be used in a marker-assisted selection scheme. Several studies using diverse approaches, breeds and nematode species have been published, and many QTL associated with nematode resistance have been detected on more than 20 chromosomal regions, as reviewed by Dominik (2005) and Bishop & Morris (2007). Some of these QTL were detected near candidate genes such as *interferon-gamma* (Coltman *et al.* 2001; Davies *et al.* 2006). However, these QTL studies have generally been performed in sheep, and only a single study has been conducted in goats (Bolormaa *et al.* 2010) using a candidate-gene approach.

The lack of investigations in goats raises the possibility of studying QTL for nematode resistance using a genome scan approach. Of specific interest is the Creole goat breed, which typically faces continual strong parasite challenge under humid tropical conditions. The Creole population is a mixture of African and European breeds, and although it is well adapted to its harsh environment, it shows genetic variability for nematode resistance. Heritability estimates for FEC and PCV (packed cell volume) in Creole goats range from 0.14 to 0.33 and 0.10 to 0.33 respectively (Mandonnet *et al.* 2001). Thus, it provides an informative model to increase current knowledge of nematode resistance in goats.

The objective of this current study was to identify QTL for nematode resistance in a Creole goat population, using several criteria for nematode resistance, including FEC, PCV, eosinophil count, body weight (BW) and immunoglobulin A and E (IgE and IgA) activity against *Haemonchus contortus* third-stage larvae and excretory/secretory products. This study should supply novel information on QTL for nematode resistance in goats.

Materials and methods

Outbred design

The Creole goat is the local breed raised for meat in Guadeloupe, in the French West Indies. An experimental flock has been reared at INRA-Gardel (Moule, Guadeloupe) since 1995 to study gastrointestinal nematode resistance. Animals are raised on pasture (*Digitaria decumbens*) all year long and are naturally exposed to mixed nematode infections. The main species infecting the Creole goat are, in order of their importance, *Haemonchus contortus*, *Trichostrongylus colubriformis* and *Oesophagostomum columbianum*. Exposure to infectious larvae varies with temperature and humidity, with the highest levels of infections by *H. contortus* being found in the rainy season (Aumont *et al.* 1997a).

Kids from the same cohort were raised together and weaned at 82 days of age on average. Anthelmintic treatment was administered every 8 weeks after weaning with

levamisole (12 mg/kg). All animals used for QTL analysis came from this population and were bred over a 5-year period (1999–2004). The population studied comprised 383 kids from 12 half-sib sire families.

Phenotypic measurements

Faecal samples were collected twice (weeks 6 and 7 after drenching) at two different ages (7 and 11 months) to determine FEC using a McMaster method modified for rapid determination (Aumont *et al.* 1997b). FEC7 and FEC11 variables were the average of these two measures at 7 and 11 months respectively. Blood samples were collected at weaning, and leucocytes were then extracted and sent to INRA's LABOGENA laboratory for DNA extraction and genotyping. Blood samples were also collected using anticoagulant-coated tubes on the 6th week after drenching for all animals at 7 and 11 months of age. Circulating eosinophils were counted at both ages, according to the method of Dawkins *et al.* (1989), on a Malassez cell counter. PCV was also measured at both ages using the capillary micro-haematocrit method. Finally, BW was measured at 210 and 325 days of age, corresponding to approximately 7 and 11 months of age. Blood samples were also collected at 11 months of age using tubes without anticoagulant and centrifuged for 5 min at 5000 rpm. Serum was then frozen at -20°C until analysis. Activity of IgA and IgE against a crude extract of *H. contortus* third-stage larvae (L3) and excretory/secretory products (ESPs) was measured by indirect ELISA based on the method used by Bambou *et al.* (2008), using the serum collected at 11 months. ESPs were prepared using adult *H. contortus* collected from the abomasa of sacrificed goats.

Genotyping and creation of the genetic map

Prior to genotyping offspring, 27 sires were tested for heterozygosity at 400 microsatellite markers (INRA and LABOGENA). These markers were chosen based on their location on either the MARC2004 cattle genetic map (Ihara *et al.* 2004) or the sheep genetic map (Maddox *et al.* 2001).

Firstly, microsatellites with the highest heterozygosity among all sires were retained. Sires with the highest percentage of heterozygosity for these selected markers were then chosen. Among these families, those with the greatest phenotypic variability based on two measures of FEC were selected. Related families were also preferred. A total of 12 sires and 101 microsatellites were then chosen based on these tests (Table S1). Then, 383 kids and 162 does were genotyped for these markers, giving a total of 552 animals (Table 1) (Note: three male kids became sires and two female kids became dams).

Table 1 Characteristics of genotyped families in the quantitative trait loci (QTL) design.

Family	Number of offspring	Number of does genotyped ¹
1	35	22 (24)
2	28	19 (21)
3	31	24 (25)
4	51	17 (28)
5	25	10 (18)
6	55	25 (34)
7	24	14 (17)
8	37	18 (24)
9	16	9 (13)
10	25	8 (16)
11	28	22 (22)
12	28	22 (24)

¹Total number of does is shown in parentheses.

Table 2 Characteristics of the genetic map.

Chromosome	Length of link group (cM)	Number of markers	Mean percentage of heterozygous sires (%)
1	172.1	4	79
2	148.9	8	70
3	142.2	7	76
4	75.6	3	75
5	107	5	70
6	110.4	8	72
7	129.5	4	71
8	100	2	83
9	92.9	3	69
10	145.6	4	56
11	98	2	67
12	80.9	4	71
13	10.7	2	63
14	67.5	4	65
15	28.1	4	75
16	100	2	63
17	90.2	4	77
18	59.1	7	68
19	13.4	2	54
20	8.7	2	83
21	74.8	4	71
22	56.4	4	69
23	66.2	3	69
24	100	2	67
26	11.5	2	79
29	63.1	5	68

Relative marker locations were established by creating a linkage map for each chromosome using CRIMAP (Green *et al.* 1990). The position of the first marker on each chromosome was always set at 0 cM. Chromosomes 2 and 6 were the chromosomes with the best coverage, with eight markers each (Table 2). The mean percentage of heterozygous sires was 70% across all markers. Four chromosomes (8, 11, 16 and 24) had only two markers, too far apart to

estimate precisely their relative positions, and consequently their linkage distances were defined to be 100 cM apart.

Data analysis

A total of 602 animals were analysed, comprising 383 kids from 12 sires and 210 does. Family size varied from 16 to 55 kids. Trait distributions were tested for normality using a Shapiro–Wilk test, and transformations were chosen to normalize the variance. Logarithm and square-root transformations were tested for all traits. FEC and eosinophil counts were log-transformed by $\ln(\text{trait} + 15)$, where 15 is half of the measurement increment for FEC. Other trait distributions were almost normal and did not require any transformation. For the QTL analysis, fixed effects were fitted using the general linear model procedure of SAS software (SAS 1999). Fixed effects tested for all traits were the cohort (37), sex (2), birth-rearing rank (3) and the type of nursing (natural or artificial). Approximate phenotypic correlations between traits were calculated using the Pearson correlation coefficient [Corr procedure of the SAS software (SAS 1999)] for transformed data corrected for environmental effects.

In addition to analysing measurements at single time points, data for FEC, PCV and eosinophil counts at the two ages were analysed using a repeated measurements analysis to create a single measurement per trait for the QTL analyses. A repeatability model was fitted using SAS software, and traits were corrected for fixed effects. In addition to the classical fixed effects, mixed models included the effect of measurement age (i.e. 7 or 11 months), and random animal and residual effects. All these effects were found to be significant. The estimates of average animal effect for FEC, PCV and eosinophil count traits were defined in the following analyses as $\text{Ln}(\text{FEC}(\text{rep}))$, $\text{PCV}(\text{rep})$ and $\text{Ln}(\text{eosi})(\text{rep})$ respectively.

Quantitative trait loci analysis was performed with QTL EXPRESS (Seaton *et al.* 2002), using regression techniques (Knott *et al.* 1996). The probability of inheriting a particular sire haplotype at a particular position was calculated at 1-cM intervals, conditional on the marker genotypes of the individual and its sire and on the sire's linkage phase. Phenotypes were then regressed on this probability and fixed effects for each trait, at every position. QTL analysis for repeated measurements was performed on the individual animal effect solutions. An F-ratio was obtained for the full model vs. the same model without the inheritance probability. The position of the QTL was indicated by the position with the largest *F*-value. Chromosome-wide thresholds, at the 1% and 5% levels, were obtained for each chromosome by permutation testing (Churchill & Doerge 1994), using 10 000 permutations for each trait and each chromosome. QTL effects were divided by the phenotypic standard deviation of each trait to be expressed in standard deviation units. The proportion of phenotypic

variance explained by the QTL was calculated as $4(1 - MS_{full}/MS_{reduced})$, where MS is the residual mean square from the regression analysis (Knott *et al.* 1996). By dividing this phenotypic value by the heritability, this results in the proportion of genetic variance (GP) explained by the QTL. As these results came from a half-sib analysis, the proportion of total additive genetic variance explained by the QTL was calculated as GP $(1-h^2/4)$. Confidence intervals for QTL were also calculated using QTL EXPRESS software with the bootstrap method. Finally, the power of QTL detection of different experimental designs was determined as a function of the number of sires, the number of offspring per sire, the heritability of the trait, the heterozygosity of the QTL, the type I error accepted, the magnitude of the QTL effect and the recombination fraction between marker and QTL (Weller *et al.* 1990).

Results

Descriptive statistics for each trait are shown in Table 3. Infection level, PCV and BW in these animals were consistent with previous results obtained from the entire experimental flock (Mandonnet *et al.* 2001). Furthermore, Mandonnet *et al.* (2001) presented comprehensive genetic parameter results for a subset of the traits investigated here, and these results are reproduced in Table S2.

Significant fixed effects were the reproductive group and sex for all traits. A fixed effect representing the rank of litter was added for eosinophil counts at 7 months of age. The type of nursing (natural or artificial) was added for PCV at 7 months and BW at both ages. Phenotypic correlations corrected for these effects are presented in Table 4. FEC and PCV were negatively correlated in both ages. A negative phenotypic correlation was found between FEC and eosinophil counts at 11 months of age, and PCV and BW were strongly positively correlated.

Significant QTL are shown in Table 5. This study identified 13 QTL, on chromosomes 1, 3, 5, 6, 7, 8, 9, 10, 14,

21, 22 and 26. Five QTL were significant at the 1% chromosome-wide threshold. As is often seen with linkage-based QTL studies, the confidence intervals for each QTL were large, being equivalent to the genotyped region in respective chromosomes. The average effect of most of the significant QTL exceeded one phenotypic standard deviation, and three QTL had a mean effect over two phenotypic standard deviations. However, because of the Beavis effect, these QTL effects are likely to be overestimated. Two QTL were found on the same chromosome (26) for FEC at 11 months of age and IgE anti-esp. However, correlated traits such as FEC and PCV were never associated with the same QTL in this study. In contrast, no QTL were detected for IgA anti-L3 or IgA anti-esp. Two QTL were significant on chromosomes 8 and 9 for repeated measurements of eosinophil counts and PCV respectively. These two chromosomal regions were also detected using single measurements for the same phenotype at 7 and 11 months of age respectively.

All half-sib families were segregating for at least one QTL, except the family of sire 4. Three families stood out, segregating for four QTL (sire 7) and five QTL (sire 6 and

Table 4 Phenotypic correlations between resistance traits at seven (above diagonal) and 11 months of age (below diagonal) and correlations between 7 and 11 months of age for each trait (on diagonal).

Trait	<i>ln</i> (FEC)	<i>ln</i> (eosi)	PCV	BW
<i>ln</i> (FEC)	0.17**	−0.03	−0.20***	−0.04
<i>ln</i> (eosi)	−0.18**	0.24***	0.30***	0.18***
PCV	−0.18**	0.12*	0.36***	0.39***
BW	−0.14*	0.05	0.52***	0.82***

* $P < 0.05$.

** $P < 0.01$.

*** $P < 0.001$.

FEC, faecal egg count; PCE, packed cell volume; BW, body weight.

Table 3 Summary statistics of nematode resistance traits.

Trait	Unit	N	Mean	SD	Min.	Max.	Mean of untransformed data
<i>ln</i> (FEC7)	<i>ln</i> (eggs/g)	399	5.99	1.39	2.71	10.90	982
<i>ln</i> (FEC11)	<i>ln</i> (eggs/g)	367	5.92	1.38	2.71	8.76	774
<i>ln</i> (eosi7)	<i>ln</i> (cells/ml)	405	6.37	1.09	2.71	8.98	945
<i>ln</i> (eosi11)	<i>ln</i> (cells/ml)	406	6.79	1.05	2.71	9.24	1409
PCV7	%	444	25.3	5.26	8.00	39.0	—
PCV11	%	420	27.3	4.67	9.00	39.0	—
BW7	kg	585	13.9	2.50	5.60	23.9	—
BW11	kg	435	18.3	3.60	7.97	26.5	—
IgA-L3	OD	314	0.32	0.19	0.03	0.74	—
IgA-esp	OD	300	0.22	0.14	0.03	0.65	—
IgE-L3	OD	315	0.28	0.12	0.04	0.60	—
IgE-esp	OD	312	0.14	0.05	0.03	0.34	—

FEC, faecal egg count; BW, body weight; IgA, Activity of immunoglobulin A; IgE, Activity of immunoglobulin E; PCV, packed cell volume.

Table 5 Quantitative trait loci (QTL) detected for nematode resistance traits.

Chr.	Trait	Position (cM)	Families segregating for QTL	Mean QTL effect (in SD)	Proportion of phenotypic variance explained by QTL	Proportion of additive genetic variance explained by QTL	Significance
22	ln(FEC7)	0	1, 10	1.17	0.23	1.83	¹
26	ln(FEC11)	3	1, 6, 9, 11	1.07	0.35	1.51	¹
8	ln(eosi7)	81	6, 8	1.34	0.26	1.15	¹
14	ln(eosi7)	67	6, 7	1.36	0.20	0.89	²
7	ln(eosi11)	0	8, 11	4.60	0.19	1.08	²
5	PCV7	27	3, 7	1.88	0.18	0.83	²
9	PCV11	76	9, 12, 6	1.56	0.18	0.75	²
21	PCV11	0	2, 12	1.24	0.18	0.73	²
6	BW7	3	2, 3, 5, 8	0.95	0.17	0.57	²
3	IgE-L3	4	6, 7, 10	1.33	0.24	0.34	²
10	IgE-L3	4	1, 7, 10	2.98	0.24	0.34	¹
1	IgE-esp	129	10, 12	2.31	0.19	0.59	²
26	IgE-esp	11	2, 10, 11	1.15	0.19	0.59	¹
8	Ln(eosi)(rep)	72	6, 12	1.88	0.16	1.83	¹
9	PCV(rep)	15	6, 12	1.55	0.15	1.51	²

¹1% chromosome-wide level.²5% chromosome-wide level.

FEC, faecal egg count; BW, body weight; IgA, Activity of immunoglobulin E; PCV, packed cell volume.

sire 10). The family of sire 7 had the lowest mean FEC and the third highest mean PCV at 11 months of age for both traits. This family also had the lowest response for IgE-esp and the second lowest response for IgE-L3. The family of sire 10 had one of the lowest FEC, highest PCV, highest BW and the lowest responses for IgA-esp and IgA-L3 at 11 months of age. IgA-esp and IgA-L3 responses were the lowest in the family of sire 6. The family of sire 6 was also the largest family in the QTL design, with 55 offspring, which is consistent with the importance of large half-sib families in the power of QTL detection as shown in Table 6. The power calculations for different designs revealed that our design had a detection power of 0.40 for the parameter values investigated, suggesting that there are likely to be segregating QTL that this study has missed. Increasing the average number of offspring per family to 90 would increase the power of detection up to 0.87.

Discussion

We previously described a significant genetic variability for nematode resistance in Creole goats and calculated heritability for FEC, PCV and BW (Mandonnet *et al.* 2001). The present study analysed the further genetic basis of nematode resistance in Creole goats by detecting QTL for eight relevant traits: FEC, PCV, eosinophil counts and BW at seven and 11 months of age and levels of IgA and IgE anti-*Haemonchus contortus* L3 crude extracts and ESP at 11 months of age. For this purpose, we sampled individuals that were representative of the entire experimental population, as the phenotypic correlations estimated are similar to those estimated in the whole population (data not shown).

Table 6 Power tests of different designs for quantitative trait loci (QTL) detection in 12 half-sib families.

Number of offspring per family	Recombinant frequency between QTL and marker		
	0.30	0.25	0.20
30	0.38	0.58	0.76
50	0.63	0.82	0.93
70	0.77	0.92	0.98
90	0.87	0.97	0.99

All designs are for a heritability of trait of 0.20, heterozygosity of the QTL of 0.50, type I error of 0.05 and QTL effect of 1 in phenotypic standard deviation.

The design used in this study allowed the detection of 13 QTL associated with nematode resistance, despite the low power of detection (40%). Therefore, there are likely to be several more QTL that this study has missed. Nematode resistance is likely to be polygenic (Kemper *et al.* 2011), with several QTL with smaller effect, rather than a few major QTL as concluded by most studies of performance traits in sheep. Therefore, some QTL segregating in this population have been probably missed owing to the lack of power. For example, the *F*-ratio for FEC11 on chromosome 9, where a QTL was found for PCV11 at 76 cM, was almost significant at the 5% chromosome-wide level for the same position. A higher power of detection may have resulted in this QTL being declared to be significant for both traits. This limited power of detection could partly explain why correlated traits such as FEC and PCV were never associated with a same QTL in this study. The analysis of repeated measurements also did not result in the detection of QTL significant for correlated traits.

However, the presence of QTL on chromosomes 8 and 9 for eosinophil counts and PCV respectively is confirmed with repeated measurements.

Most of our QTL were detected at or close to a marker position on the genetic map. Walling *et al.* (2002) suggested that the bias towards marker positions is greatest under the null hypothesis of no QTLs or when QTL effects are small. Therefore, this increases the risk that some of the QTL detected in this study could be either false positives or true QTL but with an upwardly biased estimated size of effect. A solution to allow an increase in the precision of the location and to confirm the actual presence of these QTL in our design could be to increase the number of markers on chromosomes where QTL were detected. Decreasing the expected recombinant frequency between QTL and marker from 0.3 to 0.2 in our design could increase the power of detection from 41% to 79% for a QTL of magnitude one phenotypic standard deviation unit. To obtain a similar power of detection without changing the number of markers per chromosome, an average of 40 offspring per sire should be added to our design to yield an average of 70 offspring per sire. The first solution seems more appropriate and could be achieved by using SNP technology once suitable tools become available for goats. In addition, three of the most resistant families stand out as worthy of further investigation, as they are segregating for several QTL, and further studies should focus on these families.

To our knowledge, this is the first genome scan providing evidence of genomic regions associated with nematode resistance in goats. However, a study using a candidate-gene approach has been published in Australian goats (Bolormaa *et al.* 2010), focusing on chromosome 23 using three microsatellite markers adjacent to the major histocompatibility complex (MHC). QTL associated with FEC, eosinophil counts and basophil counts were detected in two goat populations. In our study, no QTL were detected on chromosome 23; however, this chromosome was screened with only three microsatellite markers. Adding markers near the MHC may allow a comparison with the only other study currently available in goats.

Many QTL associated with nematode resistance have been detected in sheep (Dominik 2005; Crawford *et al.* 2006; Davies *et al.* 2006; Moreno *et al.* 2006; Bishop & Morris 2007; Gutiérrez-Gil *et al.* 2009; Marshall *et al.* 2009). Despite differences in terms of parasite biology, challenge type, sheep breeds and/or measured traits, some insights can be drawn from the comparison with these previous results, taking advantage of the high degree of sequence and chromosome conservation between ruminants that would allow comparative mapping (Schibler *et al.* 1998; Schibler *et al.* 2009 Maddox & Cockett 2007).

The genome scan revealed two segments on chromosome 22 and chromosome 26 with evidence for QTL linked to FEC. It is noteworthy that in sheep, Moreno *et al.*

(2006) and Marshall *et al.* (2009) detected suggestive QTL influencing FEC on orthologous ovine chromosomes 19 and 22 respectively. Evidence for a QTL for PCV was found on chromosome 9. In dairy cattle, a QTL for gastrointestinal nematode burden has also been found on orthologous bovine chromosome 9 (Coppieters *et al.* 2009). These coincident findings strengthen the support for these detected QTL.

Immunoglobulins A and E are known to be involved in nematode resistance mechanisms. Previous studies in sheep showed that IgA might be a major mechanism controlling worm length and fecundity of *H. contortus* (Strain & Stear 2001). Elevation of serum IgE following a nematode infection has been reported in sheep (Shaw *et al.* 1999), suggesting a protective function of IgE as a result of an increase in activity of the TH2 arm of the immune system. Immunoglobulin responses, mainly IgA, IgG and IgE, have already been investigated in sheep, and QTL for these traits have been detected on chromosomes 1, 3, 20 and 23 (Crawford *et al.* 2006; Davies *et al.* 2006; Gutiérrez-Gil *et al.* 2009). The potential role of these immunoglobulins in the mechanisms of resistance led us to include them in the QTL detection design. Our study detected four regions on chromosomes 1, 3, 10 and 26 associated with IgE. None of these chromosomes were associated with a significant QTL for IgE in sheep. However, QTL for FEC and worm burden were detected on the orthologous chromosomes in sheep. These findings indicate that IgE and FEC could share common genes implicated in resistance, a hypothesis supported by significant genetic correlations between IgE and FEC in our goat population (de la Chevrotière *et al.* 2012).

Quantitative trait loci on ovine chromosome 3 have been associated with FEC and IgA activity (Coltman *et al.* 2001; Beh *et al.* 2002; Davies *et al.* 2006; Moreno *et al.* 2006). This chromosome is known to carry a candidate gene, *interferon-gamma*, thought to be associated with nematode resistance (Coltman *et al.* 2001; Sayers *et al.* 2005). The gene encoding a precursor of insulin-like growth factor I is also present on this chromosome. Higher concentrations of this hormone have been detected in resistant sheep (Liu *et al.* 2007), suggesting that resistance could enhance protein anabolism in the body, thus helping to alleviate performance loss during infection. A QTL associated with PCV at 7 months was found in our study on chromosome 5, orthologous to ovine chromosome 3. Other candidate genes such as interleukins (*IL3*, *IL4*, *IL5*, *IL7*, *IL25*) are also present on goat chromosomes 1, 7, 10, 14 and 22, where QTL were found for FEC, eosinophil counts and IgE in this study. Significant QTL for FEC were also detected on orthologous chromosomes in sheep (Benavides *et al.* 2002; Moreno *et al.* 2006; Marshall *et al.* 2009). A QTL was localised on chromosome 21 in our study, and the gene encoding for IGE is also localised on this chromosome.

This study serves as proof of principle that QTL for nematode resistance are detectable in goats. However, before incorporating this information into a breeding scheme, these results must be validated in an independent sample of animals and they must also be validated using a technology that can be more easily applied within a routine breeding programme, such as a high-density SNP chip. The combination of molecular and phenotypic information could then be beneficial in improving nematode resistance in Creole goats given the low heritability and the difficulty of measurement of this trait.

In terms of experimental design, QTL associated with nematode resistance were successfully found in this study despite the low experimental power. QTL were certainly missed, especially those with small effects, and some of those found could be false positives. This could be partially overcome by the use of SNP technology, which should be available soon for the goat, across as many animals as possible. These further analyses would complement the results obtained here with microsatellite markers.

Conclusion

This study has provided an indication of QTL linked with parasitic infection in a goat population. In total, 13 QTL were found for resistant and immunological traits. Many QTL were found on chromosomes known to carry obvious candidate genes, and further work is required to determine more precisely the position of these genes and to identify other potential candidate genes. The use of a high-density SNP chip should, in principle, provide a more powerful detection of QTL, and the results obtained would complement these first results.

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Supporting information

Additional supporting information may be found in the online version of this article.

Table S1 List of microsatellite markers used for quantitative trait loci detection.

Table S2 Previously published (Mandonnet *et al.* 2001) genetic correlations between resistance traits at six (above diagonal), 10 months of age (below diagonal) and heritabilities at 6 and 10 months of age (first and second numbers on diagonal).

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Table S1 List of microsatellite markers used for QTL detection.

Chr.	Marker	Position (cM)	PIC	Chr.	Marker	Position (cM)	PIC	Chr.	Marker	Position (cM)	PIC
1	BM1312	0	0.29	7	RM006	0	0.76	18	CSRD247	0	0.86
1	BMS574	55.2	0.76	7	BMS2258	100	0.61	18	BMS2213	3.7	0.81
1	BMS2263	114.7	0.45	7	OarAE129	124.6	0.78	18	HAUT14	24.8	0.86
1	LSCV105	172.1	0.84	7	McM527	129.5	0.74	18	ILSTS002	39.6	0.85
2	DIK4469	0	0.77	8	INRA129	0	0.60	18	INRA210	45.2	0.82
2	DIK1172	8.1	0.77	8	CSSM047	100	0.63	18	DIK4823	59.1	0.87
2	OarFCB20	30	0.55	9	BM2504	0	0.59	18	LSCV030	59.1	0.87
2	ILSTS082	62.5	0.95	9	BMS1724	43.6	0.77	19	URB044	0	0.55
2	CSSM045	65.2	0.95	9	BMS1967	92.9	0.40	19	OARFCB19	13.4	0.72
2	LSCV022	68.3	0.89	10	BM3033	0	0.52	20	BMS2361	0	0.86
2	BMS778	78.1	0.82	10	TGLA378	76.2	0.52	20	BM4107	8.7	0.84
2	OARFCB11	148.9	0.81	10	BMS2641	126.8	0.64	21	BMS1117	0	0.69
3	ILSTS096	0	0.69	10	ILSTS005	145.6	0.64	21	ILSTS052	19.4	0.79
3	INRA006	14.4	0.86	11	RM096	0	0.72	21	TGLA122	61.3	0.78
3	BL41	40	0.78	11	ILSTS045	98	0.43	21	DIK4562	74.8	0.70
3	INRA023	47.4	0.70	12	BMS2252	0	0.60	22	BMS517	0	0.57
3	HUJII77	103.5	0.78	12	CSSM051	49.1	0.86	22	DIK2716	26.4	0.64
3	BMS835	116	0.73	12	INRA005	57.4	0.89	22	BMS875	51.6	0.74
3	INRA197	142.2	0.80	12	SRCRSP9	80.9	0.62	22	OARFCB30	56.4	0.76
4	MAF70	0	0.80	13	URB058	0	0.62	23	BM47	0	0.66
4	RM188	15.9	0.74	13	MCMA02	10.7	0.58	23	OLADRB3	42.1	0.77
4	OarHH64	75.6	0.71	14	CSSM066	0	0.86	23	OARHH56	66.2	0.65
5	BMC1009	0	0.51	14	ILSTS011	10.3	0.69	24	BMS2526	0	0.69
5	BMS1248	82	0.92	14	BM302	37	0.72	24	URB031	100	0.38
5	BMS772	98.7	0.87	14	BM2934	67.5	0.48	26	HEL11	0	0.79
5	MNS037	102.7	0.90	15	BMS1004	0	0.78	26	INRA081	11.5	0.80
5	BM2830	107	0.89	15	INRA224	9.1	0.88	29	ILSTS019	0	0.70
6	INRA133	0	0.88	15	MAF65	19	0.92	29	BMS1787	13.7	0.76
6	MCM53	9.6	0.88	15	BMS2684	28.1	0.90	29	MNB34	30.7	0.87
6	BM1329	20.7	0.85	16	LSCV038	0	0.77	29	McM135	34.7	0.93
6	DIK4852	34	0.93	16	HUJ625	100	0.35	29	BMS1948	63.1	0.71
6	DIK4656	39.9	0.90	17	OARVH98	0	0.86				
6	BM415	74	0.81	17	IDVGA40	53.3	0.69				
6	ILSTS087	80.8	0.82	17	BL50	68.2	0.71				
6	DIK604	110.4	0.59	17	BM1862	90.2	0.63				

Chr: Chromosome; PIC: Polymorphism information content

Table S2 Previously published (Mandonnet *et al.*, 2001) genetic correlations between resistance traits at 6 (above diagonal), 10 months of age (below diagonal) and heritabilities at 6 and 10 months of age (first and second numbers on diagonal).

Trait	$\sqrt[4]{\text{FEC}}$	PCV	BW
$\sqrt[4]{\text{FEC}}$	0.17, 0.33	-0.47	-0.03
PCV	-0.06	0.22, 0.33	0.28
BW	-0.09	0.10	0.34, 0.23

* $P < 0.05$, ** $P < 0.01$, *** $P < 0.001$

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