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Observation of Genetic Markers for Resistance to Gastrointestinal Parasites in Goats

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Abstract In many small-scale farmers and grazing systems, the biggest problem that goats face is not the shortage of feed, but the health risks and production losses caused by gastrointestinal parasites. Although such problems have long existed, they are now even more troublesome - the old method of relying on deworming drugs to solve them is becoming less and less effective at present. On the one hand, drug resistance is intensifying; on the other hand, the pressure of environmental protection and sustainability also forces people to rethink their strategies. This study systematically explored the genetic basis of goat resistance to parasites, with a focus on analyzing key genetic markers related to immune response, intestinal barrier function, and inflammatory regulation. It also reviewed the application progress of different types of markers such as microsatellites (SSR), single nucleotide polymorphisms (SNPS), and candidate genes in resistance research. And strategies such as QTL mapping, genome-wide association analysis (GWAS), and gene expression analysis were evaluated. Through case comparisons of breeds such as Boer goats, native goats, Indian Jamunapari and African Red Maasai, this study reveals the diversity of resistance genes among breeds and their specific characteristics. This study emphasizes the significance of strengthening multi-group joint analysis and data sharing, providing a theoretical basis for building an ecological and sustainable goat anti-parasitic breeding system.

Keywords Goat; Gastrointestinal parasites; Genetic resistance; Molecular marker; Mark-assisted selection

1 Introduction

In goat farming, the problem of gastrointestinal parasites has actually always existed, but the degree of impact varies from region to region.

This is not a new problem, especially in tropical and subtropical regions where the agricultural economy is supported by goats. The losses caused by parasites are always more obvious. Nematodes like the Twisted blood Lance nematode and the Trichoderma genus are not just hidden dangers. They can indeed cause a reduction in milk production, weight stagnation, and reproductive difficulties. In severe cases, they can even lead to death. Some reports even mentioned that the infection rate of such parasites in the investigated goat population exceeded 80%, which is not only worrying but also directly related to farmers' income and animal welfare (D 'amico et al., 2025). However, it cannot be generalized - different goat breeds, ages, management methods, and climatic seasons all cross-influence the degree of infection (Mpofu et al., 2022).

Traditionally, the most common approach to dealing with these parasites is medication. At the beginning, it was fine and the effect was obvious. But as time went by, the medicine was used more and more frequently and the dosage control was not meticulous enough, so the problem of drug resistance emerged. The current situation is that many conventional deworming drugs are no longer as "effective" as before, the control difficulty has increased, and the sustainability of aquaculture has also been discounted accordingly (Kalule et al., 2023; Chan et al., 2025). So, the focus began to shift to genetic resistance. Not every goat is the same. Some are naturally more resistant to parasites - and more importantly, this resistance can be inherited. If these "capable" individuals can be screened out and bred, perhaps the disease resistance of the entire population can be gradually enhanced without relying heavily on drugs (Heckendorn et al., 2017; Tsukahara et al., 2021). Now, genetic markers including SNPS have begun to play a role in identifying resistant individuals. Especially some functional genes involved in immune responses provide clearer molecular clues for breeding and also offer new support for prevention and control strategies.

This research focuses precisely on these key points. We will start from scratch to review the prevalence of gastrointestinal parasites in goats and their impact on production performance, to see exactly what are the major drawbacks of traditional drug control, and then shift our focus to genetic resistance to systematically assess its potential as a long-term solution. More importantly, we will identify and sort out the important genetic markers that have been discovered so far, and analyze their application value in actual breeding. This study aims to enhance the understanding of these resistance genetic mechanisms, promote more effective breeding strategies, improve the health of goats, increase production efficiency, and also provide a more stable and long-term path for the breeding system of small ruminants.

2 Immunological and Genetic Basis of Goat Resistance to Gastrointestinal Parasites

2.1 Immune response mechanisms of goats to major parasites

Not all goats will show the same reaction when encountering *Haemonchus contortus*. Even if the immune system takes prompt action, it doesn't necessarily mean that the effect is equally good. Two types of immunoglobulins, IgA and IgE, are often mentioned. The level of the former is related to the number of parasites in the body, while the latter is more involved in the response to larvae (De La Chevrotiere et al., 2012; Shaw et al., 2023). Interestingly, some antigens seem to be targeted simultaneously by multiple stages of immune responses without a clear stage division. Goats that are more "resistant" usually have more prominent indicators - high levels of IgA and IgE, more eosinophils, and lower FEC. It can basically be seen that their ability to control parasites is indeed stronger.

But this immune "tactic" does not rely solely on antibodies to function. Immune cells such as T cells, B cells and monocytes will also be mobilized. The transcriptome data also revealed some "operational pathways" behind this, such as the activation of inflammation-related signaling pathways like Th1/Th2 differentiation and NOD-like receptors (Figure 1) (Wang et al., 2024; Ndaba et al., 2025). In other words, the entire immune response is a multi-link linkage reaction rather than a single link fighting alone.

2.2 Overview of the genetic basis of resistance and susceptibility traits

Relying on one gene to "carry the banner"? It is basically impossible for goats to resist parasites. It is a typical polygenic trait - immune regulation, stress response, and metabolic pathways all have to be involved to some extent. A group of genes such as *CD1D*, *ITGA9*, *IL12A*, *IL13RA1*, *CD86*, *TGFB2* and *TLR4* have been pointed out to play a role in responding to *H. contortus* infection (Estrada-Reyes et al., 2019; Mpofu et al., 2022). The problem is that the effects of each of these genes are not significant, so it might be too ideal to expect a significant improvement in resistance through just one round of breeding. For phenotypic indicators such as FEC and PCV, their heritability is between 0.1 and 0.4. They can be selected, but patience is required (Heckendorn et al., 2017).

In recent years, genetic screening methods have indeed advanced significantly. Methods such as SNP typing and transcriptome analysis have become increasingly "handy" in identifying resistant alleles and have provided more precise technical tool support for the breeding process (Rocha et al., 2023). But for it to be truly put into use in production, it still needs to be carried out and iterated simultaneously.

2.3 Phenotypic indicators of resistance traits

When it comes to determining whether a goat is resistant to parasites, apart from looking at the actual infection situation, several phenotypic indicators are also very valuable for reference. The most commonly used is FEC. The lower the value, the stronger the resistance. Some genetics studies show that its range is between 0.14 and 0.40. The FEC of well-performing goats can be about half lower than that of susceptible goats (Tsukahara et al., 2021). PCV is also an important indicator, especially for *H. contortus* with blood transfusion. A high PCV indicates less blood loss and strong resistance. The two are usually negatively correlated (Onzima et al., 2017), and a PCV lower than 20% suggests possible anemia problems. Another underestimated indicator is the weight recovery rate - goats that can stabilize or quickly regain weight during infection tend to be more disease-resistant. In addition, the antigenic reactions of IgA and IgE cannot be ignored, especially the targeting reactions to parasites. If the levels are high, it can basically be determined that the animal has strong resistance. Other hematological parameters such as hemoglobin content and mean corpuscular hemoglobin concentration are also negatively correlated with FEC, which plays an auxiliary role in identifying drug-resistant individuals (Mpofu et al., 2020).

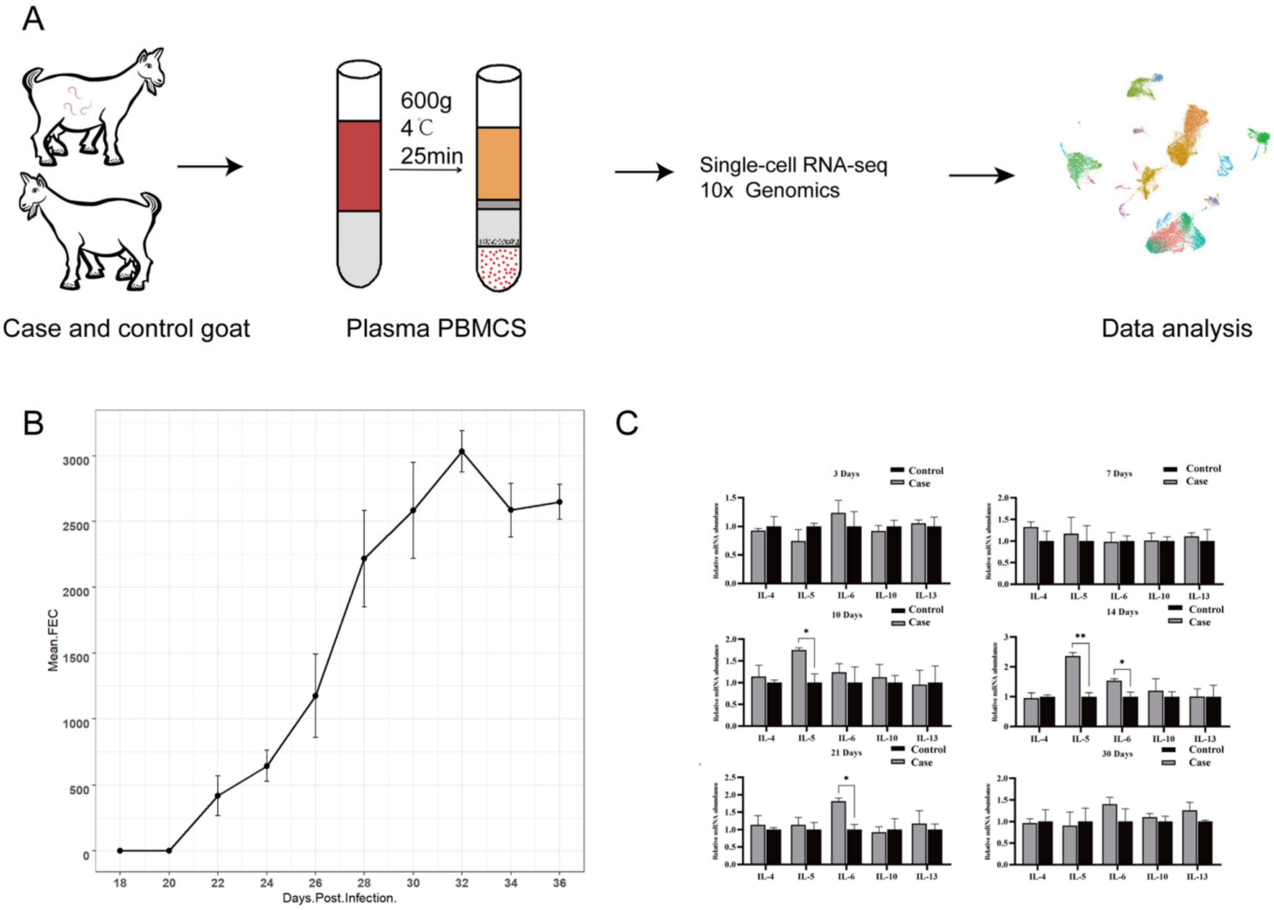

Figure 1 The change in EPG and immune gene expression. (A) Pipeline for case and control group processing and analysis; (B) EPG in goats infected with *H. contortus* at different times; (C) qPCR detection of immune gene expression in goat PBMCs at various time points postinfection with *H. contortus* (*, $p < 0.05$; **, $p < 0.01$) (Adopted from Wang et al., 2024)

3 Types and Screening Methods of Genetic Markers

3.1 Application of microsatellites (SSRs) and single nucleotide polymorphisms (SNPs) in resistance studies

When conducting resistance research, many researchers would start with SSR in the early stage. This kind of marker itself has high polymorphism and is relatively intuitive to identify. It is often used to evaluate the genetic structure of goat populations or for QTL mapping (Durigan et al., 2018). However, if more precise typing or large sample analysis is required, SNP is clearly more suitable. It is the most common type of variation in the genome and can be rapidly detected by high-throughput platforms, with much higher resolution. For instance, in studies related to egg release, SNP variations in cytokine genes such as *IL2*, *IL13* and *IFNG* have been identified, which are associated with resistance. The SNPS within the *β -tubulin isotype -1* gene of the parasites themselves, such as the Trichoderma nematode, have also been used to assess the level of drug resistance (Huang and Hong, 2025). In fact, whether it is the host or the parasite, the role of SNPS is not limited to localization, but extends to resistance monitoring and mechanism analysis.

3.2 Quantitative trait loci (QTL) mapping and genome-wide association studies (GWAS)

Not all resistance traits are easy to identify; some are very complex. At this point, QTL mapping comes in handy. Although indicators such as FEC and PCV are measurable, the distribution of gene loci controlling them is scattered. QTL scanning using SSR or SNP markers can preliminarily delineate the relevant regions (Kalaldeh et al., 2019). However, in the past, positioning relying on microsatellites was a bit crude. Later, with the maturation of SNP chip technology, positioning accuracy improved, and it was also possible to identify those QTLS that contributed little individually. In contrast, GWAS places more emphasis on statistical methods and typically seeks the association between SNPS and resistance within multiple varieties and large populations. Genes such as *CD79A* and *MAP3K7* in sheep were discovered in GWAS (Arzick et al., 2025; Costa et al., 2025). Of course, some results may be significantly influenced by the variety background or environment, and stability also needs to be further confirmed in combination with analytical methods such as RHM (Alvarez et al., 2019).

3.3 Candidate gene approach and gene expression analysis strategies

Sometimes, rather than blindly searching for variations across the entire genome, it is better to first identify those genes that are "most suspected". This is the idea behind the candidate gene method. For genes like *IL2*, *IL13*, and *IFNG*, which are known to be related to immune responses, researchers often prioritize analyzing the relationship between their SNP variations and resistance traits (Selvam et al., 2023). However, relying solely on static SNP typing is not enough. To determine whether they actually work or not, the expression levels also need to be analyzed. For instance, by using transcriptome or eQTL methods to compare the genetic differences between confrontational individuals and susceptible individuals, the activity levels in regulatory pathways can be directly observed. In recent years, an increasing number of studies have also attempted to combine GWAS with expression analysis to explore regulatory networks at the system level. In this way, the identified candidate genes are not only "possibly related", but also how they function can be known (Zhang et al., 2024).

4 Key Genetic Markers Associated with Parasite Resistance Traits

4.1 Genes related to immune responses

Not all goats react the same way when facing parasites. Some individuals exhibit a stronger immune response, which is closely related to the expression of certain specific genes in their bodies. Cytokines such as IL2, IL4, IL5, IL13 and IFNG are often associated with Th1/Th2 type immune pathways. Their high expression often corresponds to a lower number of fecal eggs, meaning that these goats are more resistant to insects (Mpofu et al., 2022). Of course, immunity is not just about the participation of cytokines. The DRB1 site of MHC Class II, as well as Toll-like receptors such as TLR2, TLR4, and TLR9, have long been proven indispensable in antigen recognition and initiating immunity. Genes like *CD1D*, *ITGA9*, *IL12A*, *IL13RA1*, *CD86*, and *TGFB2* are not significantly expressed in every sheep, but they recur in individuals classified as resistant populations (Estrada-Reyes et al., 2019; Reyes et al., 2018; 2022). In addition, the activity levels of NOD-like receptors and MAPK pathways in resistant individuals also significantly increased, indicating that the participation of these pathways in overall immune regulation is not low.

4.2 Candidate genes involved in intestinal mucosal barrier function

For parasites to enter the body, they first have to pass through a checkpoint - the intestinal mucosa. But not every time can the immune system intervene at the first moment. Sometimes, what actually determines whether the parasite can "enter" or not is this barrier itself. Goats with strong resistance seem to have intestines that are better at "guarding the door". Genes involved in tight junction structures such as ZO-1 and occludin were expressed significantly higher in such individuals, indicating that these genes contribute to maintaining mucosal integrity (Aboshady et al., 2019). Of course, merely locking the door is not enough. If the intestines are damaged, the speed of repair is also crucial. PROM1 is precisely such a restorative role, often "coming to patch up" after tissue damage. C-type lectins such as CLEC4E cannot be ignored either. They are mainly responsible for identifying invading parasites and are part of the early response system (Silva et al., 2018).

However, these are not fighting in isolation. Behind them, there is also a relatively "invisible" regulatory network - the TGF-β pathway. In particular, TGF-β1 and TGF-β2 show different manifestations in some resistant individuals. The differences in expression levels may be related to their roles in regulating immune tolerance and maintaining tissue balance. This entire set of mechanisms, to put it bluntly, is like "blocking the door" on one side and "patching the wall" on the other. Only when both actions are carried out simultaneously can the intestines have true resistance.

4.3 Genetic loci related to inflammation regulation and antioxidant defense

When goats fight parasites, many of their tissues suffer collateral damage. But not every sheep was equally intense, and there were also genetic factors behind this. Genes like *NFKBIA* and *NFKBID*, which regulate the NF-κB pathway, play a "braking" role in regulating the intensity of inflammation. NOS2 (nitric oxide synthase) will "step on the gas" when needed to help eliminate parasites (Silva et al., 2018; Wang et al., 2024). FGFBP1 is also involved in the inflammatory response and is related to the rate of tissue regeneration. Factors such as STAT5B and SOCS2, which regulate cytokine signal transduction, also frequently appear on the list of up-regulated expressions in resistant animals. It is worth mentioning that the antioxidant system has not been idle either. Under the background of oxidative stress caused by parasites, some genes that regulate the oxidative state can reduce tissue damage. Ultimately, if these genes can be utilized more effectively in breeding, perhaps the proportion of resistant individuals can be increased without sacrificing tissue integrity.

5 Application of Resistance Gene Markers and Prospects for Molecular Breeding

5.1 Feasibility of marker-assisted selection (MAS) in goat breeding

In practical operation, the traditional method of fecal egg counting is indeed not very effective - it is both time-consuming and laborious, and is easily disturbed by various environmental factors, with poor repeatability (Aboshady et al., 2019). As a result, many research and breeding projects began to turn their attention to marker-assisted selection (MAS). As long as genetic markers related to resistance traits, such as SNPS or QTLS, can be identified, the selection of insect-resistant individuals does not necessarily have to wait until adulthood, nor is it as "empirical" as relying solely on phenotypic judgment. Through DNA testing, breeders can pick out potential "good seedlings" even when the animals are still young, which also means that genetic progression will become faster and more stable (Estrada-Reyes et al., 2019). However, don't be too idealistic - compared with sheep, the progress of MAS in goats is still relatively lagging behind. This is mainly due to the lack of detailed genomic resources. Moreover, the trait of resistance itself is complex and is often determined by multiple small-effect genes, which adds a lot of difficulty to the actual breeding operation.

5.2 Challenges in coordinated selection of resistance traits and production performance

Sometimes, pest control is not the only goal. Many farmers also pay attention to growth rate, reproductive capacity and milk production, so the question arises: How to choose to have both? Theoretically, there is not much contradiction between these productive traits and insect-resistant traits - some studies even suggest that the genetic correlation between the two is relatively low and they do not affect each other (Heckendorn et al., 2017; Tsukahara et al., 2021). However, the heritability of resistance traits (such as FEC and PCV) is usually at a medium to low level, which means that relying solely on breeding methods to rapidly enhance resistance may not be realistic. One needs to be a little patient. Moreover, in practice, certain negative knock-on effects are inevitable, so the supporting monitoring work cannot be omitted. It is recommended that when making a choice, one should not only consider pest resistance but also incorporate growth and other indicators into a comprehensive selection index model for evaluation. Of course, the entire process from genotyping to phenotypic data collection is not cheap either. For regions with tight resources, it poses a considerable challenge.

5.3 Potential of precision breeding and genomic selection for parasite resistance

In the past, when it came to precision breeding, it sounded like an idealized goal. After all, for a long time, tools that could truly "see genes" were not widespread. But now the situation has changed. With the implementation of technologies such as SNP chips, GWAS, and RNA sequencing, even if the sample size is not large, relatively reliable predictive values of resistance traits can be provided (Rocha et al., 2023; Panigrahi et al., 2025). Especially in scenarios where phenotypic judgment cannot always be relied upon, these methods become particularly practical. Of course, in reality, this method cannot be immediately implemented everywhere. One prerequisite is that there must be sufficient genomic resources available, and it would be best if the cost could be even lower. Only when these conditions gradually mature can genomic selection truly enter ordinary livestock farms, rather than just remaining in the laboratories of scientific research institutions and universities.

Some people may be worried that pulling multiple traits into one model might make it more complicated. In fact, it is precisely because indicators such as pest resistance, milk production and growth rate can be considered together that comprehensive improvement can be achieved without sacrificing any one of them. This multi-objective breeding strategy sounds easy, but to truly implement it, it still requires continuous advancement in three aspects: tools, costs, and data.

6 Case Studies: Comparative Analysis of Resistance Markers in Different Goat Breeds

6.1 Resistance differences between boer goats and indigenous breeds to *Haemonchus contortus*

In fact, many studies have long mentioned whether there are differences among goats in terms of parasite resistance. Interestingly, some widely promoted breeds, such as the Boer goat and its hybrid offspring, do indeed perform more "tough" when facing the twisted blood spear nematode than local breeds like the Kachang goat. This is not based on impression but is supported by experimental data. For quantitative indicators like FEC (fecal Egg Count), under artificial infection conditions, the number of eggs in Boer goats is lower, anemia is not severe, and the development speed of the parasite body is significantly slower. A closer look reveals that the performance of male sheep is better than that of female sheep, which is quite interesting (Elieser et al., 2024).

However, this difference is not limited to the comparison between Boer and Kachan. In a different geographical context, such as Africa, a similar situation can also be observed. Like Mubende goats and East African baby goats, under the same parasitic burden, the FEC values are usually also relatively low, indicating that they have a certain degree of resistance by nature (Onzima et al., 2017). Of course, it doesn't mean that all local varieties are weak; it's just that the resistance of certain specific groups is more prominent. This is also one of the reasons why in breeding projects, Boer goats are often crossed with local breeds, using their genetic characteristics to "enhance" the resistance of local populations.

6.2 QTL comparative studies between Indian Jamunapari and African red maasai goats

Before discussing genetic resistance, it is necessary to mention the research progress of QTL. Some QTL loci found in African red Marseille sheep have also occurred in other resistant breeds, such as regions that control FEC and PCV. This overlap somewhat indicates one thing: regardless of the geographical background, certain genetic mechanisms are "universal" in the manifestation of resistance. In Indian goats, such as Jamunapari, the detection of microsatellite markers DYA and ODRB1.2 also found that they were associated with FEC and PCV indicators (Shrivastava et al., 2018). Combined with the expression differences of immune genes, such as IFNG and IL-10, the genetic basis behind resistance becomes clearer. Overall, this type of cross-variety QTL information not only reveals genetic patterns but also provides a reference path for marker-assisted selection.

6.3 SNP marker association validation based on FEC data

Not every SNP is worth paying attention to, but those highly correlated with FEC are indeed worthy of repeated verification. SNPS in genes such as *CIITA*, *ATP2A3*, *HSPA8*, *STAT5B*, *ESYT1* and *SERPING1* have been shown to be significantly associated with FEC expression in various goat populations, especially in highly resistant individuals, where their expression levels are generally higher (Figure 2) (Alam et al., 2019). Interestingly, similar phenomena also occur in the genes *NLRC3*, *NLRC5*, *HIP1* and *LRP8*, and some haplotypes at these loci are often associated with resistance (Omar et al., 2019). Importantly, these results are not only present in one experiment or one region, but can also be reproduced across regions and varieties, which endows these SNPS with higher application value in breeding. Incorporating them into the breeding strategy might be an effective entry point for enhancing population resistance in the future.

7 Conclusions and Future Perspectives

Over the past few decades, research on goats' resistance to gastrointestinal parasites has gradually accumulated, but this path is far from over. As is known to all, this type of resistance is a rather complex trait that cannot be determined by just one or two genes, especially when it involves genes closely related to immunity such as MHC, IFN-γ, various interleukins, TLR, and T-cell receptors. However, to be on the other hand, although quite a few QTLS and SNPS have indeed been identified, each one, when viewed individually, does not have a significant impact. As for phenotypic indicators such as FEC, PCV and immunoglobulin, they remain the most commonly used selection tools. However, if these can be combined with genetic markers, the selection may be more accurate and faster. Recently, genomic approaches such as transcriptomics, RNA sequencing, and GWAS have continuously brought about new clues. For instance, TGF-β, the MAPK pathway, and cell adhesion molecules have all been drawn into the resistance network. Molecular means for resistance breeding do seem to be a reliable path now, and both MAS and genomic selection hold promise.

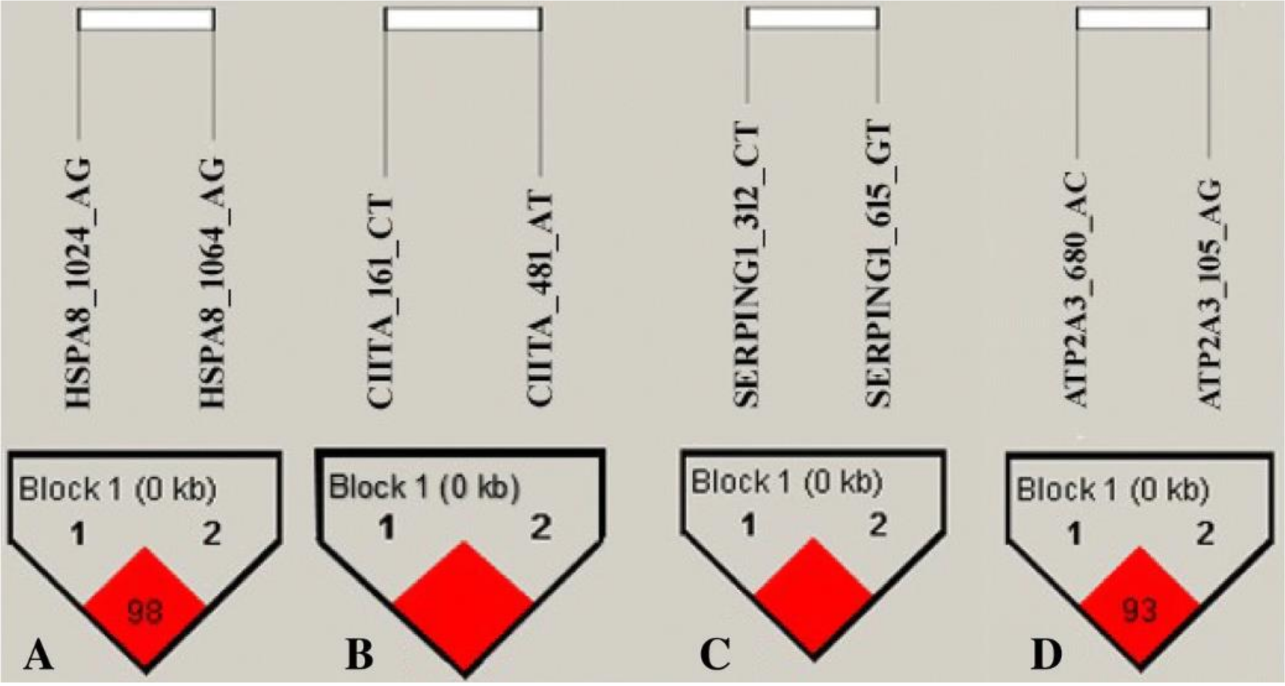

Figure 2 Linkage disequilibrium blocks for SNPs in four genes: a *HSPA8*_1024_A > G and *HSPA8*_1064_A > G (LD = 98, $r^2 = 0.98$); b *CIITA*_161_C > T and *CIITA*_481_A > T (LD = 100, $r^2 = 1$); c *SERPING1*_312_C > T and *SERPING1*_615_G > T (LD = 100, $r^2 = 1$); d *ATP2A3*_150_A > G and *ATP2A3*_680_A > C (LD = 93, $r^2 = 0.93$) (Adopted from Alam et al., 2019)

However, to be fair, compared with sheep, the research foundation in this area of goats is still a bit weak. There are too many variables such as different species, climate and parasitic stress. Many research results do not match each other and the data lack uniformity. It is precisely for this reason that to identify truly "universal" genetic markers, it is necessary to integrate data across groups and regions. Multi-center collaboration and data sharing are inevitable directions. In fact, some studies have already attempted to borrow the genomic resources of sheep. After all, they are not completely similar to each other, which can save a lot of verification costs.

For breeding practice, relying solely on molecular markers is far from enough. A more realistic approach might still be to combine the labeling information with traditional phenotypic data, and add indirect indicators like FEC or PCV to build a more precise selection system. Of course, this also needs to be combined with reasonable feeding management, especially in reducing the use of deworming drugs. After all, the problem of drug resistance can no longer be ignored. If breeding strategies only pursue resistance, they may also neglect other traits, such as growth or reproductive ability. Therefore, when selecting and breeding, it is also necessary to pay attention to maintaining genetic diversity and not make the population "narrow". The next key point is not only to continue expanding the genomic data of goats, but also to consider developing some low-cost and highly efficient molecular detection tools. More importantly, it is to facilitate cross-border collaboration, enabling these research achievements to truly leave the laboratory and play a role in different countries and different breeding systems, and promoting the real implementation of goat resistance breeding.

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Conflict of Interest Disclosure

The authors affirm that this research was conducted without any commercial or financial relationships that could be construed as a potential conflict of interest.

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