Genetics of Parasite Resistance in Small Ruminants

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Introduction

Since the detrimental influence of internal parasites in small ruminants is substantial world-wide, all possibilities for countering those effects should be considered seriously. Use of anthelmintics cannot be the only option; there is appropriate concern about the development of resistance to the effects of anthelmintics by internal parasites. If climate change is a reality, we should expect corresponding changes to influence the demographics of internal parasite populations, although predicting those changes will never be simple. Genetic control strategies through the hosts (small ruminants) are appropriate for consideration. The objective of this paper is to discuss the possibilities to genetically influence small ruminant traits related to internal parasites.

Broad Aggregate of Genotypes = Breeds

Somewhere in history, livestock breeders began to use genetic principles that resulted in the formation of breeds or races. In those early years breeders were to some degree isolated; the ability to add unrelated animals to their flocks or herds was limited. This resulted in the concentration of alleles (versions of genes) identical by descent (inbreeding). These breeds were strongly influenced by geography and became adapted to the conditions that they and their ancestors lived in. Many of these breeds are maintained today as well, and those adaptation attributes acquired through their history are still valuable today for livestock producers. The simple use of genetics to affect traits of importance constitutes **breed selection**. There are documented breed differences in resistance to the effects of internal parasites. Examples of breeds with greater resistance (relative to other breeds) to gastrointestinal nematodes include Florida Native, St. Croix, Gulf Coast Native, Red Maasai (Kenya), Santa Inês (Brazil), and Katahdin.

Crossbreeding

Maybe the greatest advantage of crossbreeding is the generation of heterosis, also known as hybrid vigor, for many economically-important traits. Heterosis is defined as the mean difference of crossbred animals relative to the weighted mean of the pure breeds that are present in the crossbred animals. It is experimentally calculated as

$$Heterosis = Crossbred\ mean - Purebred\ mean$$

For example, in Table 1, values are given for means of 3 traits in Suffolk, Gulf Coast Native, and first crosses ($\mathbf{F_1}$, the **filial 1** generation). Li et al. (2001) detected significant heterosis for packed cell volume (PCV) and fecal egg count (FEC). The value for FEC, though numerically negative, is favorable: crossbred lambs had lower FEC than the average of the purebred lambs.

Table 1. Breed group means and estimates of heterosis for blood packed cell volume (PCV) and fecal egg count (FEC) at 20 wk age in lambs (adapted from Li et al., 2001)

Group	Packed cell volume	Fecal egg count
Suffolk	18.2	7,289
Gulf Coast Native	25.5	952
Purebred average	21.85	4,120.5
F_1	26.1	1,966
Heterosis, trait units	4.25	–2,154.5
Heterosis, % PB avg	19.4%	–52.3%

Can heterosis be used to improve parasite resistance in small ruminants? It looks like it; however, we should be careful in its interpretation. Sometimes heterosis can be detected in harsh environments primarily because one parent breed is not well-adapted to the environment, drastically influencing the purebred mean. For example, in the Louisiana results in Table 1, the Suffolk means for PCV and FEC are extremely unfavorable relative to the other breed groups. The F_1 FEC mean is much higher (worse) than the Gulf Coast Native, yet enormous heterosis was detected. In this case, if we were only considering this trait, we should compare the F_1 to the Gulf Coast Native. However, heterosis favorably influences other traits, especially reproduction, and the value of heterosis across all traits should benefit the entire production system. Heterosis may not always be favorable; an example in beef cattle production would be that heterosis for birth weight could result in larger calves at birth and consequently greater calving difficulty and death loss.

Selection

First consider a hypothetical quantity **individual genetic merit** for a trait of choice. This value is not palpable or observable, but we assume that every animal that could be considered a potential parent has such a value for our trait of interest. If we knew these values, we would rank the potential parents by these values. Statistical regression on an individual's **phenotype** (record for the trait we are considering) can be used to estimate these values. Since the 1960s, livestock breeders have utilized a statistical tool Best Linear Unbiased Predictions (BLUP) for estimating genetic merit for individual animals, which include pedigree information and records of relatives. The more records used in these analyses the more accurately genetic merit can be estimated. These estimates of genetic merit (**expected progeny differences**, EPD) represent differences among mean values: the expected mean of an individual's progeny minus the population mean.

These EPD are estimates of additive genetic merit and are therefore highly dependent upon the **heritability** of the trait. Heritability (h^2) represents the proportion of trait variation that is caused by the additive genetic variance. Heritability ranges theoretically from 0 to 1, and higher values result in more accurate estimation of EPD. Typical values for common traits in livestock, e.g., weight or milk production traits range from 0.2 to 0.4

Could parents be identified to improve traits related to internal parasite resistance using this methodology? Yes. Estimates of heritability for such traits can be seen in Table 2.

An important result from this work is that selection for improvement of FAMACHA© score is possible using EPD, since h^2 in this Merino flock in South Africa was as high as the more expensively measured traits: hematocrit values (PCV) and FEC.

Table 2. Estimates of heritability from analyses of moderate and peak worm challenge data in which records from treated lambs were either excluded or penalized (adapted from Riley and Van Wyk, 2009)

	Excluded	Penalized
Moderate worm challenge		
FAMACHA©	0.08 ± 0.04	0.11 ± 0.04
Peak worm challenge		
FAMACHA©	0.19 ± 0.054	0.25 ± 0.054
Hematocrit	0.21 ± 0.059	0.22 ± 0.058
Fecal egg count	0.19 ± 0.061	0.23 ± 0.065

Estimates of heritability appear to be dependent upon the worm environment, that is, the severity of the worm burden to which animals are exposed. In this study, moderate and peak worm challenge levels were determined by the number of lambs requiring treatment. Estimates of heritability were largest under severe worm challenge environments. A harsh environment permits differential expression of resistance by animals, allowing identification of superior individuals; obviously, it would be undesirable to permit a flock to deteriorate under severe challenge just to facilitate that identification. Because there was a strong genetic correlation of FAMACHA© scores taken in harsh and moderate environments EPD values can be generated under less than severe worm challenge environments and still achieve effective selection. Equally important results from this work were the strong genetic correlations of FAMACHA© with hematocrit value and FEC. This implies that selection for FAMACHA© would result in favorable correlated response in both other traits.

The necessity of treatment of individual lambs to minimize economic loss will influence the kind of genetic analyses employed. Treatment dramatically improves the worm environment of those individuals that are treated, and consequently the traits measured, to their advantage relative to untreated lambs. In the process, valuable information is generated about the genetic merit for lamb resistance, but typically such records are excluded from genetic analyses. Numbers of observations are reduced, and the treated animals and their relatives are unfairly advantaged, resulting in incorrect estimation of genetic merit. Penalization (using a scheme for altering observed records based upon treatment status and date), rather than exclusion, may be a better way to incorporate valuable resistance information into genetic analyses. Inclusion of penalized records increased the estimates of heritability from these data (Table 2).

Genomics

Tremendous effort has been expended in the last decade to incorporate genomic information in livestock improvement programs. At this point, it should be difficult to claim success.

Traits controlled by a single (or a few) gene. Examples include the callipyge and the Booroola Fecundity (FecB) genes in sheep, and the coat color genes such as Melanocortin 1 Receptor in cattle. Traits that fall into discrete categories (double-muscled vs. normal muscling) are often controlled by one or a few genes. Most of these are easy to identify and we know specifically the different **alleles** (versions of the gene) and can identify the **genotypes** (allelic content at a gene = 2 alleles) of individuals. Many of the tests that genetic companies offer are limited to these types of traits, e.g, scrapie susceptibility.

Traits controlled by a large number of genes, each with a small but cumulative contribution to the trait. Traits that are continuous (measured on an infinitely-divided number line; e.g., body weight) in nature are often controlled by many genes. In many cases there is probably a subset of genes that are mostly responsible. These are more difficult to identify, and especially arduous to establish **causation** (that is, the actual genes responsible are known and mapped).

In most cases **markers** (physical modifications of sequence of nucleotides, which are the building blocks of DNA, within the genome), rather than the causative genes themselves are tracked. One especially helpful marker is the **single nucleotide polymorphism** (SNP). If we could have enough SNP located across the **genome** (the genome consists of the DNA present across all 27 and 30 pairs of chromosomes in sheep and goats, respectively), then we could assume that the causative genes would be **linked** (located near enough to each other on the chromosome that the recombination process that normally occurs in the formation of sperm and ova seldom separates the two) to the SNP, and we could therefore monitor the inheritance of the unseen, unknown genes with the seen, known markers.

The development of high density SNP arrays (like the OvineSNP50 BeadChip http://www.illumina.com/products/ovinesnp50_dna_analysis_kit.ilmn) has greatly facilitated investigation of these concepts. Annealing DNA from a single animal to a chip that has short target sequences of nucleotides for over 50,000 SNP **loci** (plural of **locus**, which is a physical place in the genome) would result in learning the genotypes at all of those SNP. Genotypes are then statistically associated with trait variation using regression theory, and estimates of that association at each locus are produced. Those estimates (or a subset of the most strongly associated) can be summed into a single value representing genetic merit for a trait. Researchers in dairy production in the United States, Europe, and Australia are probably most involved in this process (**genomic selection** using **molecular breeding values**—a breeding value is an EPD doubled) at the moment. There are a number of serious issues that could influence the validity of these, and there has not been pronounced success in this area. It is appropriate to be cautious with adoption of selection using such values today, but there is potential that this could impact selection of small ruminants for parasite resistance. Regions on two sheep chromosomes have been detected as associated with resistance to *H. contortus* (Marshall et al., 2012).

All the Easy Research Has Been Done

Our opinion is that it is worth the effort to document gene expression in some body tissue relating to a specific trait and then assemble genotypes for that gene and predict genetic merit using those rather than markers. Probably all of our efforts as geneticists to date are naïve, that is, things are considerably more complex than we ever thought. Without doubt, EPD today have value that can be used to successfully select parents. We have very bright people working on implementation of genomic information into predictions of genetic merit for livestock. However, we could never imply that we are on the verge of accomplishing this.

References

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