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REVIEW

Resistance and resilience to diseases in local ruminant breeds: a focus on South America

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SUMMARY

Interest genetic variability loss has taken importance not only the production but also because it may have negative effect on the epidemiology of animal diseases. Livestock activity can present considerable periodic economic losses due to animal disposal, reduced productivity, failure to express the genetic potential of animals, treatment costs, labour and professional assistance, closing of trade due to sanitary barriers and competition with foreign markets. Thus, disease resistance is a desired attribute in livestock production and animal health may be limiting in cattle production systems. Some confusion in terminology exist: resistance is defined as the ability of the host to exert some degree of control over the pathogen's life cycle, while tolerance defines the impact of infection on animal performance. A concept very close to tolerance is resilience, which can be defined as maintaining the animal's productive capacity in the face of infection. There are numerous reports indicating local breeds as an important reservoir of naturally genetics resistance to disease as a process of adaptability to the environment. Referring to the main diseases of domestic animals (tuberculosis, brucellosis, foot-and-mouth disease, etc.), numerous genes have been identified and studied as biomarkers for resistance and tolerance like the BOLA complex, CD, NOD and SLC11A1 genes among the most important. Although the limiting factor for breeding programs to include genetic disease resistance is the need to quantify resistance phenotypes. This can be expensive and logistically difficult, and is a significant barrier to selection for disease resistance. For this reason, disease resistance characteristics are an attractive target for genomic studies and are generally the subject of these studies.

Resistencia y resiliencia a las enfermedades en las razas de rumiantes locales: un enfoque en América del Sur

Palabras clave
Raza local.
Sanidad animal.
Zoonosis.
Tolerancia.
Adaptabilidad.

RESUMEN

La pérdida de variabilidad genética de interés ha tomado importancia no sólo la producción, sino también porque puede tener un efecto negativo en la epidemiología de las enfermedades animales. La actividad ganadera puede presentar considerables pérdidas económicas periódicas debido a la eliminación de animales, la reducción de la productividad, la falta de expresión del potencial genético de los animales, los costes de tratamiento, la asistencia laboral y profesional, el cierre del comercio debido a los obstáculos sanitarios y la competencia con los mercados extranjeros. Por lo tanto, la resistencia a las enfermedades es un atributo deseado en la producción ganadera y la salud animal puede estar limitando en los sistemas de producción de ganado. Existe cierta confusión en la terminología: la resistencia se define como la capacidad del huésped para ejercer cierto grado de control sobre el ciclo de vida del patógeno, mientras que la tolerancia define el impacto de la infección en el rendimiento animal. Un concepto muy cercano a la tolerancia es la resiliencia, que se puede definir como mantener la capacidad productiva del animal frente a la infección. Existen numerosos informes que indican las razas locales como un importante reservorio de resistencia genética natural a las enfermedades como un proceso de adaptabilidad al medio ambiente. Refiriéndose a las principales enfermedades de los animales domésticos (tuberculosis, brucelosis, fiebre aftosa, etc.), numerosos genes han sido identificados y estudiados como biomarcadores de resistencia y tolerancia como los genes BOLA, CD, NOD y SLC11A1 entre los más importantes. Aunque el factor limitante para que los programas de reproducción incluyan resistencia a enfermedades genéticas es la necesidad de cuantificar los fenotipos de resistencia. Esto puede ser costoso y logísticamente difícil, y es una barrera significativa para la selección de la resistencia a las enfermedades. Por esta razón, las características de resistencia a la enfermedad son un objetivo atractivo para los estudios genómicos y generalmente son objeto de estos estudios.

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INTRODUCTION

Unexplored genetic material of plants and animals is a potential force for food security and sustainable development in every production system. This material is critical for ensuring the resilience and flexibility of production systems, as well as for increasing their production. It has been argued that global food security. Therefore, global food security can be achieved and

maintained through the proper use of genetic resources (Hatab, Cavinato & Lagerkvist 2019; Sansoucy 1995). Humans use approximately 40 domesticated species of animals to meet their needs for food, clothing, and transport, among others. From these species, 4500 breeds have been developed, which are known as the global animal genetic resources. Each breed has a unique set of genes and it is estimated that approximately 30% of them are threatened with extinction (Zhang et al. 2018). The threat of inefficient use, especially in developing countries, is arguable even more serious than the threat of extinction. The United Nations Food and Agriculture Organization (FAO) has been urged by member countries to manage the global animal genetic resources. Recent progress in this area has been fast, but capacity is limited; therefore, priorities have to be set for conservation and development programs of local breeds (Barker 1999). Ensuring sufficient genetic variability in animal populations is essential for adaptation to future climatic changes, for meeting the demands of consumers, and for the continuous genetic improvement of economically important characteristics of livestock. Unfortunately, the current trend is decreasing genetic variability, both within and between breeds. One of the causes for reduction in genetic variability among various breeds is the reduction or extinction of local-breed herds. Lower productive indices have been the key factor for the loss of local breeds, as they are being continually replaced by high-yield cross-border international breeds (Biscarini et al. 2015). Reducing genetic variability may also have a negative effect on the epidemiology of animal diseases Springbett et al. (2003). Resistance to or tolerance of disease may be among the most valuable characteristics of local farm animal breeds with a view to increased sustainability of farm production, and may have great potential as alternative tools for disease control (FAO 2010). The aim of this review is to clarify the terminology that describes the phenomena linked to genetic mechanisms of defense and domestic animal's response to diseases. We perform besides an extended review of the state of art in some of the main livestock diseases with special attention to the south American and Tropical area.

DISEASES AND THEIR MECHANISMS

Livestock diseases causes significant and recurrent economic losses due to the discarding of animals, reduced productivity, failure to express the genetic potential of animals, treatment costs, labor and professional assistance, and trade closure due to sanitary barriers and competition with foreign markets (MAGA. 2006). Thus, disease resistance is a very desirable attribute in livestock production (Julian 2006).

Endemic and introduced infectious diseases represent the greatest challenge because they cannot be controlled using traditional techniques. Examples of global significance include tick and nematode infestations, where resistance to both acaricidal and anthelmintic drugs is widespread. Thus, alternative or complementary control strategies are needed; among these is the increase in host resistance to infection or disease (Bishop & Woolliams 2010).

As a first step, it may be possible to improve the genetic resistance of ruminants to most diseases by selective breeding for disease resistance character, although the exact determination of resistant phenotypes under natural and field conditions is still challenging. For a subset of diseases, it may be feasible to measure a phenotype that identify the disease resistance in sufficient numbers of animals to determine resistant genotypes, and it has been shown to be economically feasible to incorporate such characteristics into selection programs (Davies et al. 2009). In cattle, promising results have been obtained with mastitis and, more recently, with tuberculosis and paratuberculosis (Bishop & Woolliams 2014).

Hosts and microorganisms can interact in numerous ways along a continuum of possibilities, where the extremes are represented by mutualism and parasitism. These interactions may result in a wide range of events, such as the elimination of the host-associated microorganism, the death of the host, states involving latency and commensalism, and the development of disease in the host (Fagundes 2011).

The interaction of the immune system with infectious agents occurs in a highly dynamic manner, with sophisticated control and escape mechanisms. Understanding this complexity is a prerequisite for establishing infection control. Although the immunological responses developed to control various infections are often specific to the disease, they often exhibit mechanisms common to most infections. A priori mechanisms may be redundant, but there is a large range of subtle host-parasite interactions, which determine the establishment or absence of disease.

In principle, hosts can employ two different strategies to defend against parasites: resistance and tolerance. Animals usually exhibit considerable genetic variation for resistance. However, little is known about the development of tolerance. It is important to distinguish between these two components because, by definition, resistance has a negative effect on parasites, whereas tolerance does not; as a result, their relative importance will have substantial consequences for the ecology and evolution of parasite-host interactions (Råberg, Sim & Read 2007).

The terminology used in the field provides a further cause for confusion in this topic. Specifically, the generic term "disease resistance" is not appropriate because it implicitly confuses infection, which is the invasion by a pathogen or parasite, with the negative condition that is the consequence of infection (Bishop & Woolliams 2014).

Resistance is best understood from the ecological approach of viewing it as an interaction between the host and the pathogens (Grenfell & Dobson 1995). It may be defined as the host's ability to exercise some degree of control over the pathogen's life cycle (Bishop 2012; Bishop & Stear 2003). In other words, resistance is linked to the host's ability to limit its parasite load (Råberg, Sim & Read 2007). This broad definition has the benefit of encompassing the various forms of resistance that can be developed by hosts, such as reducing the possibility of infection, reducing pathogen prolife-

ration after infection, reducing pathogen elimination or infection transmission. It is also important to recognize that the concept of resistance is more relative than absolute. A change in a given host's resistance can affect the population in general, since some changes only benefit the host, while others, such as a reduction in infection rate, benefit other members of the population, too (Bishop & Woolliams 2014).

The genetic characteristics of the resistance mechanism are those that are regulated by the genes acting as barriers to the entry of pathogens and the genes that are expressed during the innate immune response or the acquired immune response, which both result in the reduction of the pathogen burden. The genes and molecular pathways associated with resistance are expressed primarily in the mucosal and innate immune systems, which control the events that occur soon after the invasion of pathogens. Resistance genes encode the receptors involved in the uptake of pathogens, as well as the pattern recognition receptors (PRRs), such as the family of Toll-like receptors and molecules involved in the intense and rapid inflammatory responses that lead to the rapid clearance of pathogens without the production of immunopathology (Glass 2012).

Tolerance can be defined as the net impact of a given level of infection on the animal's performance, considering the performance as a regression in pathogen load (Bishop 2012). Therefore, tolerance represents the ability of the host to limit the damage caused by a particular parasitic load (Råberg, Sim & Read 2007). Tolerance can also be understood as the host's ability to maintain homeostasis even in the presence of pathogens in replication, with a consequent limitation of aggression (Doeschl-Wilson & Kyriazakis 2012).

Resilience is a concept that is very close to tolerance. It can be defined as the maintenance of reproductive capacity of the animal during infection (Bishop, S. C. 2012). Clunies-Ross et al. (1932) was the first researcher to recognize the distinction between "resistance to infestation" and "resistance to the effects of infestation". Albers et al., considers that few researchers have taken this distinction into account. It is important to emphasize that clarity must be maintained in separating the concepts of resistance (the ability to suppress infection) and resilience (the ability to maintain reproductive indices relatively unchanged in the presence of infection/infestation) (Albers et al. 1987).

Genetic characteristics of tolerance are conferred by genes that suppress or limit active host responses to the pathogen and/or genes that prevent pathogen-mediated toxicity, without having an effect on the pathogen burden. Candidate genes for tolerance include pattern recognition receptors (PRRs), unidentified pathogen growth sensors, as well as genes associated with host metabolism changes and intrinsic molecule-associated risks. In addition, the genes that control the regulatory pathways related to tissue repair and healing should be considered (Glass 2012).

Resistance and tolerance may have similar impacts on the health and reproduction of individuals in the face of a given disease, but they can have contrasting effects on the performance, risk, and severity of the disease in the population as a whole. For example, raising host resistance may result in the successful eradication of a disease from a population of animals; however, this may be more difficult if the hosts have high tolerance, since they may harbor the pathogen without showing obvious signs or symptoms of the disease. Conversely, it has been argued that increased host resistance can stimulate the conflict between the host and the pathogen, encouraging the pathogen to become more virulent. In contrast, increased tolerance imposes no or little selection pressure on the pathogen. Furthermore, while the mechanisms of disease resistance may be specific to a particular pathogen (for example, development of antibodies specific to that pathogen), tolerance mechanisms, such as the repair of damaged tissues, are associated with the host and are not necessarily specific to the pathogen. Tolerance mechanisms are thus more likely to be generic and apply to a variety of pathogens. Therefore, improving tolerance may be more beneficial if the population is exposed to a variety of pathogens or strains, or in cases where disease eradication has proved difficult (Doeschl-Wilson & Kyriazakis 2012).

In contrast to evolutionary biology and plant breeding, animal breeding has only recently begun to seriously consider the distinction between resistance and disease tolerance, and its consequences. Therefore, it is urgently necessary to deepen the understanding of the mechanisms for improving one or both of these host defense mechanisms (Doeschl-Wilson & Kyriazakis 2012).

GENETICS AND DISEASESES

The major histocompatibility complex (MHC) exists in almost all vertebrates. Its molecules are central to the immune system, functioning as specific markers that confer individual identities to cells. The MHC is a region of the genome with a dense cluster of genes that exhibit a high degree of polymorphism, which is key to the innate and adaptive immune responses, playing an important role in the host's response to pathogens (Kelley, Walter & Trowsdale 2005). The generic name given to the protein group encoded by the MHC genes depends on the species. In cattle, it is known as the bovine leukocyte antigen (BoLA) system and is located on chromosome 23. In sheep, it is called the ovine leukocyte antigen (OLA) system, located on chromosome 20. In goats, it is called the leukocyte goat antigen (CLA) system, located on chromosome 23. Finally, in buffalo, it is called the buffalo leukocyte antigen (BuLA) system and is located on chromosome 2 (Vandre et al. 2014).

The MHC and its genes can be divided into 3 major classes: Class I, Class II, and Class III. Class I MHC genes encode glycoproteins that are expressed on the surface of almost all nucleated cells; their main function is the presentation of antigenic peptides to cytotoxic T lymphocytes. Class III MHC genes encode, in addition to others, several proteins with immunological functions, including components of the complement system and molecules involved in inflammation. The MHC Class II region encodes the α and β chains that

form the Class II heterodimers. There is a high degree of polymorphism within Class II genes. The α and β chains are membrane glycoproteins. Unlike Class I MHC molecules, they are not ubiquitously expressed; they are displayed on the surface of antigen-presenting cells (APCs), including macrophages, dendritic cells (DC), and B lymphocytes (Cresswell 1994). In addition, Class II MHC genes are expressed in other cells in response to interferon gamma (IFN-γ) (Steimle et al. 1994).

Both chains α1 and β1 contribute to the structure of the peptide binding site. The peptide binds to the cleft and the residues that cover the cleft make contact with the peptide. The residues are the most polymorphic elements, which in turn determine the chemical structure of the cleft and influence the specificity and affinity of the binding peptide. Class II peptides are generally 13 to 25 amino acids long, but the cleavage of Class II molecules is opened on one side so that it can accommodate longer peptides (30 or more amino acids), with some amino acids located on the side of the crack. Anchor sites for one or more amino acids also exist in the cleft of the Class II MHC molecule (Trowsdale 1995).

The α2 and β2 chains are largely non-polymorphic. During the presentation of antigen to $CD4^+$ T lymphocytes, the helper molecule binds to the β 2 domain of MHC class II molecules. MHC class II genes are associated with disease resistance and are extremely polymorphic in most vertebrates (Trowsdale 1995).

In ruminants, a large rearrangement within the *MHC class II* region led to the division of the region into two distinct sub-regions: classes *IIa* and *IIb.* In turn, class *IIa* also has two sub-regions, one composed of the *DR* family genes (*DRA* and *DRB*) and one by the *DQ* family genes (*DQA* and *DQB*). These gene products, DR and DQ molecules, are the primary class II restriction elements for the $CD4^+$ T cell helper (Aida 1995; Glass & Jensen 2007).

The sub-region composed of the DR genes has been thoroughly studied, due to the large number of polymorphisms present as well as its functional importance (Dongxiao & Yuan 2004). In cattle, the DRA gene has only one allele that encodes the α-chain of the DR molecule, that is, it is a monomorphic gene (Amills et al. 1998; Takeshima & Aida 2006). DRB genes encoding the β-chain of the DR molecule are highly polymorphic; the exhibited polymorphism is mainly in the second exon, which is responsible for encoding the variable portion of the peptide-binding site of the protein (Amills et al. 1998). There are at least three DRB genes: DRB1 (a pseudogene); DRB2, which is poorly expressed; and DRB3, which is highly expressed and polymorphic (Kumar et al. 2011). DRB3 is functionally the most important of the three (Takeshima & Aida 2006). The genes of the DRB family have aroused the interest of researchers seeking to improve disease control methods in animals of economic interest; they are mainly used for the development of new vaccines and the selection of resistant animals (Niranjan et al. 2010; Vandre et al. 2014). In cattle, the BoLA-DRB3 gene is the most polymorphic Class II locus and influences the specificity of the epitope and thus the magnitude of the antigenic response of the T lymphocyte in infectious diseases (Takeshima & Aida 2006).

The DQ region comprises five DQA loci and four DQB loci, with the highly polymorphic genes DQA1, DQA2, DQA3, DQB3, and DQB2 (Takeshima & Aida 2006). To date, a total of 56 DQA alleles have been described (http://www.ebi.ac.uk/ipd/mhc/bola/). The DQ region is unique in cattle in its complexity, with approximately half of the known haplotypes of duplicate DQ genes (Andersson & Rask 1988; Ballingall, Luyai & McKeever 1997), and the DQA and DQB polymorphism being related to the duplication of DQ genes. The main function of the DQ molecule is the preparation of the CD4+ T-cell response (Glass & Jensen 2007).

The polymorphisms of the MHC gene have been extensively studied in ruminants of several local breeds in particular in cattle, sheep and less in goats, these include: Creole cattle from Latin America (Giovambattista et al. 2013); Argentine Criollo cattle (Giovambattista et al. 1996; Giovambattista et al. 2001); Bovine Colombian Crioulo (Martínez, R et al. 2005) (Hernández, D. Y. et al. 2013); Hanwoo, Korean beef cattle (Lee et al. 2012); (Miyasaka et al. 2011; Miyasaka et al. 2012), (Takeshima, S et al. 2008) (Takeshima, S. et al. 2003); native Filipino cattle (Takeshima, SN et al. 2014); native Iranian cattle (Firouzamandi et al. 2010); Norwegian cattle (Mejdell et al. 1994); African cattle (Ballingall, Luyai & McKeever 1997); Indian cattle (De, Singh & Brahma 2011; Pipalla et al. 2004); and goats (Amills et al. 2004); sheep (Valilou et al. 2015).

Other classes of molecular markers of disease resistance in local breeds are also being evaluated, e.g., The natural resistance-associated macrophage protein (NRAMP), which is a protein associated with natural resistance that is expressed only in the lysosomes of macrophages and monocytes. NRAMP has recently been renamed as SLC11A1 - solute carrier family 11 members 1 (Cortés & González 2015).

LOCAL BREEDS AND DISEASES

There are numerous reports on the increased resistance to disease presented by local breeds in environments where livestock is heavily challenged. When countries enter information on breeds of farm animals in the FAO Information System (DAD-IS), they have the opportunity to indicate whether the breed has any particularly interesting or important characteristics, including disease resistance. In most cases, the information entered for specific breeds has not been the subject of scientific research. However, for many infectious and parasitic diseases, information is available in the scientific literature that supports an increased resistance and tolerance to disease in local breeds. Examples are the West African N'Dama trypanotolerant cattle, or East African Red Maasai sheep, with their high resistance to gastrointestinal worms. **Table I** describes the diseases and the corresponding species of resistant and/or tolerant ruminants recorded in DAD-IS (FAO 2010).

The most obvious and widespread way of using genetic resistance is the continued use of local breeds in

the regions in which they are adapted. Although there is a lack of scientific evidence for all breeds, the theoretical and empirical evidence available is consistent with the hypothesis that virtually all local breeds are sufficiently resistant/tolerant to the endemic diseases of their regions, as they have continued to produce and reproduce in their environment. Exotic breeds brought to a region tend to be more susceptible to its endemic diseases, unless such exotic animals come from regions where the same diseases are present (Garcia 2011). Exotic breeds sensitive to endemic diseases will only succeed in competition with the local breed when the production system is altered so that the spread of disease can be prevented or its effects can be substantially mitigated. An example is the use of European dairy breeds and their crosses for milk production in some areas of the tropics where, despite the high susceptibility of most tropical diseases, they remain productive with the use of vaccination and therapeutic control. Another example is the use of various trypanosome-susceptible breed in South Africa and elsewhere in Sub-Saharan Africa where the challenge of trypanosomiasis has been eliminated by the destruction of the tsetse fly habitat (Gibson 2002).

Genetic resistance has been observed for the major classes of pathogenic organisms: prions, viruses, bacteria, as well as various classes of eukaryotic parasites; several local breeds have been found to be resistant to a number of endemic diseases at the same time. However, this may be a more widespread phenomenon than is currently known, since most breed have only been tested for one disease (Gibson 2002). Another complicating factor is the fact that identifying the disease-resistant phenotype is difficult. It is false to assume that in a population of sick and healthy animals all healthy animals are disease resistant. Some sensitive animals may not have been sufficiently exposed to the pathogenic organism to become ill. Animals that look healthy may have subclinical infections, functioning as pathogen reservoirs. Often, the clinical manifestation of a particular disease can be confused with another similar disease, because the exact diagnosis of the disease is often costly and time-consuming. For example, pneumonia can be confused with bronchitis, emphysema, pleurites, pulmonary adenomatosis, upper respiratory infection, or pleural fibrosis. The success of genetic selection for disease resistance depends on the correct identification of the disease-resistant phenotype (Snowder 2006). All of these barriers explain the difficulty for researchers in clearly defining the mechanisms of resistance, tolerance, and resilience of local breeds.

Table I. Number of ruminant races reported to DAD-IS as showing resistance or tolerance to specific diseases or parasites (Número de razas de rumiantes reportadas a DAD-IS que muestran resistencia o tolerancia a enfermedades o parásitos específicos**).**

Disease	Bufalo	Cattle	Goat	Sheep
Tripanosomiasis		17	4	4
Ticks infection	1	17		1
Ticks transmitted diseases (unspecific)		4		
Anaplasmosis		2		
Babesiosis		4		
Heartwater/Cowdriosis (Erliquiosis)		1		1
Gastrointestinal parasites	1	2	1	9
Fascioliasis	2			2
Bovina Leucosis		9		
Pododermatitis		1		14

TUBERCULOSIS

Bovine tuberculosis (TB) is a chronic respiratory disease caused by *Mycobacterium bovis*. Its control and eradication have been based on the detection and elimination of infected animals, as well as transport restrictions. With the decrease of responsive cattle to tuberculin tests, it was observed that some cases of tuberculosis occurred through contact with wild species, which serve as disease reservoirs. Regardless of the source of infection, many animals are exposed to and infected by the pathogen rarely exhibit clinical signs, carrying the subclinical infection over an extended period. This makes it difficult to detect the disease in a flock. The mechanisms that cause some exposed animals develop lesions and clinical signs while others do not, are referred to as susceptibility and resistance to tuberculosis: this can be due that infection resistance is controlled by various genes (Allen et al. 2010).

Results of a study comparing the local breeds Curraleiro Pé Duro (*Bos taurus* breed) from Brazil and Nellore (*Bos indicus* breed) indicated that Curraleiro has more responsive capacity to *M. bovis*. BCG vaccination demonstrated a better resistance profile in this breed for combating intracellular infectious agents and a higher humoral non-specific and specific immune response to *M. bovis*. This was characterized by a greater number of leukocytes and higher concentrations of non-specific and specific immunoglobulins (Wolf 2009). A better cellular response was also observed in Curraleiro calves compared to Nellore animals, measured as the yeast phagocytosis ability as well as homogenous and sustained production of nitric oxide (a microbicidal substance) by macrophages derived from peripheral blood mononuclear cells in response to a vaccine. The lymphocyte cytometric analysis demonstrated that Curraleiro calves had more Tγδ cells; furthermore, CD4, CD8, and IFN-γ production by CD4 and CD8 T cells was found to be more efficient in Curraleiro animals, specifically and non-specifically (Maggioli et al. 2013).

Response to the tuberculin test may be used for identifying the resistant or susceptible phenotypes in animals. However, some individuals are found to not have any lesions during a post-mortem inspection, while other animals that do have the characteristic lesions do not test positive in the test (Doherty & Cassidy 2002). These individuals can be classified as resistant as follows: 1) test-negative individuals exposed to tuberculin but showing no clinical signs and no positive culture that are resistant and eliminated the pathogen

by the innate immune response, so they do not develop the hypersensitivity reaction; 2) test-positive individuals without clinical signs and no positive culture that are resistant to the disease due to the acquired immune response; 3) test-positive individuals without clinical signs, but with a positive culture that are in the latent phase of infection; 4) test-positive individuals without clinical signs but with a positive culture that are in the active phase of infection prior to the development of clinical signs; and 5) test-positive individuals with clinical signs and a positive culture that have an active infection and installed disease (Barry et al. 2009; Young, Gideon & Wilkinson 2009)(Allen et al. 2010).

The search for candidate genes for resistance to bovine tuberculosis is focused on the gene encoding protein 1 macrophages associated with natural resistance (*Nramp1*), which has already been described in humans and mice. This gene has also been associated with resistance to brucellosis; the resistant allele was found to be associated with macrophage survival of M. bovis BCG (Qureshi, Templeton & Adams 1996).

Studies have indicated a genetic factor in the response to infection by intracellular pathogens. This can help to identify genes that would be responsible for the resistance of certain animals or humans to infection. This type of genetic resistance manifests itself in the early stage of infection, when the resistant macrophages show an increased ability to control the replication of agents, determining the course of the infection. Genetic resistance or innate susceptibility to infection by *Brucella abortus*, *Salmonella dublin*, *Salmonella typhimurium,* and *Mycobacterium bovis* was experimentally tested in mice and it was found that the susceptibility is mediated by macrophages influenced by the *Nramp1/Slc11a1* gene, whose function is to control the intracellular replication. The gene can be studied in other species because of the high homology of murine *Nramp1* with beef (86% similar) and human (88.6% similar) *Nramp1*. Studying the *Nramp1/Slc11a1* gene can help us to understand the immune system and the ability of the protein to confer resistance. In a study on Chinese cattle for example, the authors investigated the associations between SLC11A1 polymorphisms and susceptibility to tuberculosis (TB) in Holstein, using a case-control study of 136 animals that had positive reactions to TB tests and showed symptoms and 96 animals that had negative reactions to tests and showed no symptoms. Using a logistic regression approach was found that SLC11A1-SNP1, SLC11A1-SNP3, and SLC11A1-SNP5 were significantly associated with susceptibility/resistance to TB. Haplotype analysis showed that nine haplotypes were potentially resistant to TB (Liu et al. 2017).

It can also allow researchers to study the inhibition of intracellular bacterial replication, granuloma formation, production of reactive oxygen products, the processing of antigens and the expression of a larger set of Class II histocompatibility molecules, increased fusion of phagolysosomes, and TNF and IL1 regulation. This makes it possible to understand the response to tuberculosis better and to try to select genetically resistant individuals (Herrera 2016).

The BoLA MHC gene is associated with several diseases in cattle and the variation in T cell response to *M. bovis* (Allen et al. 2010). With the help of INRA111 and BMS2753 markers, two genomic regions that were strongly associated with the reaction to the tuberculin skin test were identified using a study of 384 cattle with 160 positive skin tests (Allen et al. 2010; Driscoll et al. 2011).

Resistance is also connected to breed. It has been shown in a study of 2500 zebus, 1900 crossbred cattle, and 900 Holstein cattle that the prevalence of TB was higher in Holstein cows, which also showed greater severity of disease in test-positive animals. Thus, it was suggested that *Bos taurus* is more susceptible to TB than *Bos indicus* (Ameni et al. 2007). In Uganda, it has also been reported that the incidence of TB was 17% in the Ankole breed cattle and only 0.9% in Zebu (Hutt 1960).

Even if a great number of genetic marker have been proposed as promising tools against TB it is clear that the mechanisms involved in the infection and the host response are complex and depends on four factors, namely microbiological, ecological, immunological, and genetic (Casanova & Abel 2013). Besides one key field of study that still require elucidation is resistance to either initial infection or, after infection, resistance to progression to disease (Moller et al. 2018).

Genetic variation influences resistance and its contribution can be estimated by heritability (h^2) (Falconer & Mackay 1996). According to a study that evaluated the variation of the genetic response to TB in deer, it was observed that approximately 48% of the variation in response to *Mycobacterium bovis* was related to the host's genetic factors (Allen et al. 2010). In cattle, studies have also been carried out evaluating the heritability of resistance to TB through a correlation between susceptibility of *M. bovis* infected animals and the response to a tuberculin test with purified protein derivatives (Bermingham et al. 2009).

There is, however, a problem with diagnostic tools: when selecting individuals that do not respond to the tuberculinization tests, we could be inadvertently selecting individuals that can become infected, but are not detected due to a lack of response to the diagnostic test. Thus, selection of unresponsive animals would indirectly select animals resistant to the external signs of infection by *Mycobacterium* sp. (Allen et al. 2010).

To make the selection of TB resistance using heritability, it is necessary to know how this parameter is estimated. One genome-wide association study (GWAS) using single-nucleotide polymorphisms (SNPs) estimated a 21% heritability of TB resistance in a Holstein-Friesian breed, attributed to 2 potential new loci containing candidate genes on chromosomes 2 and 13. Two significant SNPs (rs136617760 on chromosome 2 and another on chromosome 13) are found near the *PTPRT* gene linked to the protein tyrosine phosphatase receptor subfamily, which are essential for the regulation of signaling pathways (Bermingham et al. 2014).

Field studies underestimate the heritability of resistance because the response to the pathogen occurs in different forms in different animals, and because

diagnostic tests are not sensitive enough to identify all positive animals. The understanding of the resistance to bovine TB requires an understanding of how the organism infects the host and how the host and the pathogen respond to immune activity. These interactions are studied to understand which candidate genetic loci are involved in the immune response and the resistance (Allen et al. 2010).

BRUCELLOSIS

Bovine brucellosis, caused by the bacterium *Brucella abortus,* is another important zoonotic disease under mandatory sanitary control in many countries; it causes damage to reproduction and milk production. To select animals resistant to brucellosis, polymorphisms in the gene *Slc11a1* (formerly *Nramp1*) have been investigated. The gene encodes a transmembrane transporter located in the phagolysosome, which contributes to the bactericidal activity of macrophages. In cattle, natural resistance to *B. abortus* is associated with polymorphisms in the microsatellite 3'untranslated region (3'UTR) of the *Slc11a1* gene, but the association between this polymorphism and natural infection remains controversial (Paixão, Martinez & Santos 2012).

Martínez *et al.* (2008) studied three polymorphisms in the gene *Slc11a1* (SNP4, 5, and 6). These polymorphisms were investigated in naturally or experimentally infected animals. Heifers were inoculated via conjunctival with the virulent *B. abortus* strain 2308 during pregnancy after artificial insemination; heifers that subsequently gave birth without complications were considered resistant. It was observed that naturally infected susceptible cows were often homozygous for the polymorphism, exhibiting the CC genotype in SPN4, and AA in SPN5. These results can support genetic selection of resistant animals (Paixão, Martinez & Santos 2012).

In small ruminants, the presence of the alleles A15 and B7/B7 3'UTR of the *Slc11a1* gene has been identified in animals with a lack of specific antibodies against *Brucella melitensis* (Iacoboni et al. 2014).

The association between resistance to brucellosis and this gene was investigated in Colombian creole breeds of *Bos taurus* and *Bos indicus*. The Creole cattle breed (*Bos taurus type)*, Blanco Orejinegro breed, showed a high frequency of GT12 (homozygous AA in the region 3'UTR). The AA and AB genotypes were found to be ten times more resistant than the BB genotype (found only in the Zebus breed), indicating that this allele may be associated with resistance. The study found that homozygous BB animals had a higher index of bacterial survival in macrophages (Martinez et al. 2008).

In an experiment on the survival ability of the *B. abortus* strain Cumbal 1, isolated from a bovine, it was shown that the Colombian local cattle breed Blanco Orejinegro was more resistant to infection that Brahman Zebu cattle. Both the purebred Blanco Orejinegro and the crossbreed with the local Zebu showed lower growth of bacteria in macrophages. The crossbreed with local Zebu showed higher levels of resistance and was more capable of reducing bacterial survival. While 44% of the animals in the Orejinegro group were found to be resistant, only 21% were resistant in the Zebu group, and 60% of the crossbreed animals were resistant. The mechanism for greater control of bacterial survival in macrophages may be related to the NRAMP1 protein, which modifies the biochemical properties of the phagosome. This proves that a large part of resistance control is determined by genetic components, which can be selected in breeding programs (Martínez, R et al. 2005).

Recently seven single-nucleotide polymorphisms (SNPs) located in the PTPRT gene were associated with resistance to *Mycobacterium bovis* infection in cattle. Rossi et al. (2017) in case-control study to test if polymorphisms at PTPRT intron 8 might influence the resistance or susceptibility to *Brucella* infection in goats, DNA samples from 22 seropositive (cases) and 22 seronegative (controls) for brucellosis, found that in four previously reported polymorphisms (SNP1: rs643551276, SNP2: rs651618967, SNP3: rs662137815 and SNP4: rs657542977) and a new SNP (SNP5: chr13: 691695526) TTCCT haplotype was associated with absence of *Brucella*-specific antibodies (ORs=0.019 to 0.045).

SALMONELLOSIS

One of the factors that control resistance to intracellular microorganisms such as Salmonella is the *Nramp* gene product, a protein associated with natural resistance of macrophages. This protein controls the replicative capacity of these bacteria in macrophages in the initial phase of infection. In cattle, several works find alleles (175, 177, 179, and 181 bp) of the microsatellite, linked to *Nramp* that are associated to resistance to intracellular microorganisms (Paixao et al. 2006). For bovines, *Salmonella dublin* serves as a model for studying natural resistance to other intracellular bacteria such as *B. abortus*, since it has been shown that resistant bovine-derived macrophages effectively control the growth of both bacteria (Paixão et al. 2007). In Colombia, it was proposed that the local cattle breed Blanco Orejinegro (BON) is resistant to infectious diseases, including brucellosis. When the *Nramp* genotypes of BON cattle resistant to *Salmonella dublin* were assessed, it was found that 98.75% of the cattle of this breed were homozygous for the resistance allele (R) and only one animal was found to be heterozygous (Martínez, Rodrigo et al. 2010).

PODODERMATITIS

Pododermatitis is caused by the coexistence of two anaerobic gram-negative bacteria, *Fusobacterium necrophorum* and *Dichelobacter nodosus* (or *Bacteroides nodosus*). While it mostly affects sheep and goats, it can also affect cattle, deer, and horses. Generally, sheep are affected more severely than goats (Pezzanite et al. 2009).

Pododermatitis occurs most frequently in temperate zones, and there is evidence that some breeds are more resistant than others (FAO 2010). A study

conducted in Australia revealed that when exposed to natural infection on irrigated pastures, the British breeds Romney Marsh, Dorset Horn, and Border Leicester showed lower susceptibility to contagious pododermatitis (manifested by relatively benign lesions and faster resolution) than the Peppin and Saxon Merino breeds (Emery, Stewart & Clark 1984). Likewise, crossbreed East Friesian × Awassi sheep had a lower prevalence of the disease when compared to purebred Awassi during an outbreak of the disease in Israel (Shimshony 1989). It seems that breeds that originated in wetland areas, where the disease is more common, are less likely to be susceptible (FAO 2010).

ENZOOTIC BOVINE LEUKOSIS (LEB)

Enzootic bovine leukosis (LEB) is a major disease with a considerable negative impact on zootechnical and economic indexes. It is a chronic infection caused by a virus of the family Retroviridae, the bovine leukemia virus. Retroviruses, like the bovine leukemia virus, are so named because they transcribe the viral RNA into DNA to migrate to the cell nucleus and integrate into the host genome (Balvay et al. 2007).

The pathogenesis of the bovine leukemia virus infection clearly involves host immune factors, including MHC products (Nagaoka et al. 1999). Resistant alleles of the BoLA DRB3.2 gene (*1101, *2709, and *20012) were observed more frequently in Colombian creole cattle compared to susceptible alleles, conferring a relatively low occurrence of leukemia in this breed despite the high prevalence of the disease in the country (Hernández, et al. 2011). Polymorphism of the DRB3 gene can be considered an important factor in the slow progression of the disease in Harton Criollo del Valle, where the alleles *1101 and *2703 were found to be associated with low levels of virus infection, low development lymphocytosis, elevated antibodies to leucosis and low proviral load. The alleles are considered resistant to the development and/or progression of the disease. On the other hand, the allele *1701 was negatively associated with the above traits, and was therefore classified as sensitive to this disease (Hernández, Álvarez & Muñoz 2014).

Genetic selection of bovines based on the DRB3.2 gene alleles associated with bovine leukosis resistance appears to be a promising additional tool for controlling the spread of the virus. However, a potential risk of the expansion or segregation of the BoLA gene is that it could increase susceptibility to other common viruses, since the strong association between low proviral load and low antibody titer against major structural proteins of leucosis does not provide a response. The humoral immune response is important in preventing diseases such as foot-and-mouth disease, IBR, and BVD. However, no association was found between the BoLA DRB3 gene polymorphism and the titers of neutralizing antibodies against foot-and-mouth disease virus, bovine viral diarrhea virus, and herpesvirus 1 (Nagaoka et al. 1999). On the other hand, another study confirmed the strong association between BoLA DRB3.2 and low antibody titers against structural proteins, the best leukosis resistance marker. This may confirm that the selection and segregation of leukosis-resistant alleles, besides resulting in genetic improvement and control of the disease, would not affect resistance and/or predisposition to IBR, BVD, and foot-and-mouth disease (Juliarena et al. 2009).

FOOT-AND-MOUTH DISEASE (FMD)

Foot-and-mouth disease (FMD), also known as *Aphthae epizooticae*, is a highly contagious disease affecting domestic and wild artiodactyls, such as cattle, sheep, goats, buffalo, deer, antelope, and swine (House & House 1999). It is economically devastating because it can severely restrict the national and international trade of cattle and their products (Marques et al. 2015). The typical clinical signs of FMD are vesicular lesions in the feet, buccal mucosa, and mammary glands of the females, which can cause sialorrhea (excessive salivation), lameness, and fever. Therefore, this disease cannot be clinically differentiated from other vesicular diseases. The virus is usually transmitted through the milk, meat, or saliva of a diseased animal, remaining alive in the bone marrow even after the death of the animal. Indirect transmission can occur in many ways, either through physical contact or mechanically (Sutmoller et al. 2003).

Members of the cell receptor family integrins (V1, V3, V6) have been identified as factors in adhesion of different viruses to host cells. In the case of the FMD virus (FMDV), integrins bind to the cell recognition site in the Arg-Gly-Asp (RGD) tripeptide sequence located on the virus VP1 protein. Genetic evidence of this interaction has been obtained by mutating the RGD sequence into infectious cDNA clones, identifying non-infectious viral particles unable to bind to susceptible cells. Some natural genetic resistance to the FMDV has been found in Blanco Orejinegro cattle, and it has been suggested that some degree of resistance could be caused by mutations in these cellular receptors responsible for virus adhesion (Rodríguez & Ariza 2006).

A study carried out *in vitro* on the presence of resistance to FMD in Blanco Orejinegro (BON) cattle in Colombia found that the presence of phenotypic polymorphism in animals infected with A24-Cruzeiro serotype (93.2%) was higher when compared to animals infected with serotype O1-Campus (56%). It is believed that the different serotypes have different mechanisms for penetrating the cells, which determines the susceptibility to each of them. Although both require interferon and αV-b3 integrin, the O1-Campus serotype may also be able to utilize other integrins and heparin sulfate, which would increase its virulence. One of the ways to determine the susceptibility of the animals is to evaluate the production of type I interferon and the relative absence of the αV-β3 integrin before the animal is subjected to FMDV infection (López et al. 2000).

ECTOPARASITES AND THE DISEASES TRANSMITTED BY THEM

Tick infestations are important not only because of their negative impact on the physical state of the organism or toxicity, but also because of the transmission of

"bovine sadness complex" agents such as *Babesia bovis*, *B. bigemina,* and *Anaplasma marginale*. In practice, incorrect or indiscriminate use of acaricides can accelerate the process of evolution of resistance to different drugs, allowing the occurrence of multiple or cross-resistance. The selection of resistant insect populations has been occurring not only in ticks, but also the horn fly (*Haematobia irritans*), since, due to the non-specificity of the great majority of the products used, the control of one species tends to affect the susceptibility of the others (Gomes, Koller & Barros 2011).

Phenotypic characteristics of bovine coats such as the length, thickness, texture, and color of the hair, influence their susceptibility to tick infestation and are related to the important mechanism of genetic resistance of the host (Mapholi et al. 2014). Resistance of bovine breeds to certain endo and ectoparasites can be investigated by analyzing gene expression patterns in different macrophages in producing differences in the surface molecules of uninfected cells in relation to infected monocytes, which affects their interaction with other cells, such as T lymphocytes (Glass & Jensen 2007). These differences in gene expression patterns may identify the polymorphism of candidate genes, so genomic association studies may provide valuable information for improving tick control (Mapholi et al. 2016). Genetic resistance of cattle can be used as a strategic tool to control ticks in production systems, reducing the levels of infestation in animals and the environment (Biegelmeyer et al. 2015).

Some studies have shown that tick saliva contains molecules that impede the development of the innate and adaptive immune responses, thus facilitating vector blood suctioning and transmission of pathogen, (Brake & Perez de Leon 2012). It is well documented that the local African breed N'Dama shows greater resistance to ticks than Zebu animals (Claxton & Leperre 1991; Mattioli et al. 1993; Mattioli et al. 1995). Bovines of the Brazilian local breed *Crioula Lageana* show greater resistance to ectoparasites, with fewer severe infestations by larvae of *Dermatobia hominis* and *Boophilus microplus*; this was shown to be associated with other breed characteristics, such as thinner hair (Cardoso et al. 2014).

Bovine parasite sadness is a disease caused by protozoa of the genus *Babesia* and bacteria of the genus *Anaplasma*; its clinical manifestations are fever, anemia, hemoglobinuria, jaundice, anorexia, emaciation, and high mortality among susceptible cattle (Kessler & Schenk 1998). *Bos indicus* bovines were found to be relatively resistant to infections caused by the protozoan *Babesia bovis* when compared to crossbred *Bos indicus* × *Bos taurus* cattle (Bock et al. 1997).

Studies in western Uganda, Africa, involving several *Anaplasma* and *Erlichia* species in Ankole and *Bos taurus* cattle, reported that the degree of infection was strongly associated with the animal breed, with local breeds less affected (Muhanguzi et al. 2010). Researchers studying *Anaplasma marginale*, *Babesia bigemina,* and *Theileria* species correlated genetic diversity in local cattle breeds from different agro-ecological zones in Ghana with quantitative differences in the prevalence of co-infection by these agents. They found evidence of the breed influencing the ability to resist co-infection by various pathogens (Beckley 2013).

Theileriosis is a disease of acute, subacute, or chronic evolution. It particularly affects ruminants and is characterized by symptomatic fever, enlarged lymph nodes, anemia, and pale mucous membranes (although, unlike *Babesia*, it rarely causes hemoglobinuria), anorexia, diarrhea, and cachexia (OIE, 2009). In the case of theilerioses caused by *Theileria annulata*, Sahiwal calves, a breed native to India, have been shown to be less negatively affected by the parasite than Holstein-Friesian calves (Glass & Jensen 2007).

In animals, the symptoms of trypanosomiasis due to *Trypanosoma congolense*, *Trypanosoma vivax*, or *Trypanosoma brucei* (the most common pathogenic trypanosomes in Africa) include anemia, fever, tearing, edema, and progressive slimming leading to cachexia and death if left untreated. Tripanotolerance has been observed in West African cattle and has been defined as the ability of some ruminant breeds to survive and reproduce, in tsetse-fly-infested areas, where other breeds cannot live without the use of chemical drugs (Berthier et al. 2016).

Tsetse-transmitted trypanosomiasis is one of the most important animal health problems in Africa; it occurs mainly in West and Central Africa as well as parts of East Africa. Other types of trypanosomiasis pose significant problems both in Africa and in other tropical regions. Resistance of the parasite associated with control programs using trypanosomicidal drugs, as well as sustainability issues involved in the implementation of tsetse control programs, have increased the interest in the use of integrated control methods, including the use of tolerant ruminant breeds (Agyemang 2005). The most trypanotolerant breeds include West African N'Dama and Shorthorn cattle, as well as Djallonke sheep and goats. Despite their smaller size, studies have shown that these breeds are more productive under moderate to high tsetse exposure than larger, more susceptible breed (Agyemang et al. 1997).

ENDOPARASITES

Gastrointestinal infections are the most important ruminant diseases in the world, especially for small herds (Perry et al. 2002). Their control is today a major problem, because the techniques used are almost entirely based on the frequent use of anthelmintic drugs. This method is increasingly considered unsustainable, due to the evolution of parasites resistant to multiple drugs. Thus, the need for alternative control methods is reinforced by the low rate of discovery of new active anthelmintic principles (McManus et al. 2014).

The evolution of resistance to anthelmintic drugs is unavoidable, as each time one of these products is administered and the animal eliminates sensitive parasites, it inadvertently selects for some resistant parasites that remain in the body and pass their resistant genes to the next generation (McManus et al. 2014). Therefore, interest in integrated parasite-management programs has been increasing. The improvement in genetic resistance to microorganisms is an important component of such potential programs (McManus et al. 2014) and can be combined with agroecological techniques (Tixier-Boichard et al. 2015).

Applying this information to the study of resistance, tolerance, and resilience of local ruminant breeds, these animals are expected to be more resistant or resilient to helminthiasis because they have gone through a longer period of adaptation at their place of production (Carvalho 2010; Ramos & Mariante 2011). This is especially true in the tropics, where the chance of an infestation with high parasitic load is higher (Sato et al. 2014). It has been found that some ovine local breeds (Crioula Lanada and Santa *Inês* sheep breeds) were more resistant than exotic breeds to gastrointestinal nematode infections (Amarante et al. 2004; Bricarello et al. 2004).

Studies evaluating helminth resistance in Red Massai ewes and Small East Africa goats, local breed on Kenya's sub-humid coast, compared them to Doppler sheep and Galla goat, and found that the local breeds were more resistant to gastrointestinal parasites (Baker et al. 2001). Red Maasai sheep are estimated to be two to three times more productive than Dorper sheep, under the same parasite environment conditions (Baker et al. 2001). This is due to an alteration in the alleles of the genes of this breed. This fact is worthy of attention because the genetic and immunological basis for this situation is relatively simple and the introduction of this allele into other breeds could bring great benefits to goat breeding around the world. The introduction of these beneficial alleles could be done by conventional genetic improvement, with long-term gene introgression, or by transgenesis (Chiejina & Behnke 2011).

Concerning the genetic improvement in resistance to parasites, the challenge is to determine the best methods of using genetic variation to reduce the consequences of parasitic diseases (Stear & Murray 1994). One option is the identification of genes that are influenced by the innate and acquired responses to the parasite, and ensuring their transfer to future generations (Pfukenyi & Mukaratirwa 2013). The identification of these genes has been performed in several species (Hunt 2011), and some genetic markers in bovine species have already been reported the scientific literature (McManus et al. 2014). Some markers related to the inflammatory response to gastrointestinal nematode infections have been evaluated, including several types of interleukin receptor genes (IL-2, IL-4, IL-12p35, IL-13), interferon gamma (IFN- Γ), and membrane cofactor protein 1 (MCP-1), which are related to decreased amount of nematode eggs per gram of feces (Anthony et al. 2007).

There is also some scientific evidence of resistance or tolerance to the hepatic parasite *Fasciola gigantica*, which is a very widespread parasite. One such example is Indonesia's Thin Tailed sheep, which were found to be more resistant to *F. gigantica* than St. Croix and Merino sheep (Roberts et al. 1997).

DISEASE-RESISTANT LOCAL BREEDS

Table II is a list the local breeds of ruminants with reports of resistance or disease tolerance.

Source: [1]Maggioli et al. (2013), [2]Vásquez-Flores et al. (2006), [3]Ameni et al. (2007), [4]Martínez et al. (2008), [5]Gibson et al. (2002), [6]Saldarriaga et al. (2000), [7]FAO (2010), [8]Hernández et al. (2011), [9]Hernández et al. (2014), [10]Rodríguez & Ariza (2006), [11]Claxton & Leperre (1991), [12]Mattioli et al. (1993), [13]Mattioli et al. (1995), [14]Cardoso et al. (2014), [15]Kessler & Schenk (1998), [16]Bock et al. (1997), [17]Glass & Jensen (2007), [18]Agyemang et al. (1997), [19]Amarante et al. (2004), [20]Bricarello et al. (2004), [21]Roberts et al. (1997).

FINAL CONSIDERATIONS

The last two decades have been marked by the development of advanced technologies and knowledge production involving genomics and epigenetics. To realize the full benefit of these technologies, pedigree flocks of local breeds in developing countries need to be established, and their performance needs to be recorded. Breeding programs need to access and use genetic information about local breed or breed combinations in production systems, especially the available information on the resistance and tolerance to disease. It is also important to consider the selection environment, the environment in which the animal will develop, and the environment where it will express its reproductive characteristics. The possibilities are enormous and tend to become more important as the animals are genetically enhanced to achieve higher levels of performance and efficiency (Scholtz et al. 2013).

Epigenetic mechanisms may explain why some breeding programs, where lines of animals are developed and selected in ideal environments (which are very different from the environments where the animals are intended to live), have been unsuccessful. Improved knowledge of epigenetic mechanisms may in the future lead to close cooperation between the breeders and the market, so that commercial selection of animals is performed with consideration of the different environments (nutrition, management and specific climate) to which the animal will be exposed; this would result in greater production efficiency (Scholtz et al. 2013).

A limiting factor in breeding programs, which include genetic resistance to disease as a selection parameter, is the need to quantify the resistance phenotypes. This can be expensive and logistically difficult, and is a significant barrier to selection for disease resistance. For this reason, disease resistance characteristics are attractive and frequent subjects of genetic studies. The benefit of the genomic approach is its ability to select the animals based on their DNA, which removes the need to expose them to infection in challenge tests, or observe their performance during a natural epidemic. The genomic approach can be accomplished if the major resistance genes or quantitative trait loci (QTL) are identified, or if chips are developed with SNP-based genomic predictors. With methods currently available, the accuracy of selection will depend on routine challenge testing or the continued presence of diseases in the field, to allow the calculation of genetic values based on the phenotypic expression of resistance (Bishop & Woolliams 2014).

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Table II. Lists the local breeds of ruminants with reports of resistance or disease tolerance (Listado de las razas locales de rumiantes con informes de resistencia o tolerancia a enfermedades).

Disease	Local breed with some report in genetics resistance
Tuberculosis	Bovino - Curraleiro Pé-Duro[1], Bos indicus[2,3]
Brucelosis	Bovino - Blanco Orejinegro4[4], East African Shorthorn Zebu[5]
Salmonellosis	Bovino - Blanco Orejinegro[6]
Pododermatitis	Bovino – Sayaguesa[7] Ovino - Beni Ahsen[7], Beni Ahsen[7], Large Tailed Han[7], Small Tailed Han[7], Kamieniecka[7], Leine[7], Swiniarka[7], Polskie Owce[7], Dlugowelniste[7], Churra[7], Lebrijana[7], Lacha[7], Bündner[7], Oberländerschaf[7], Engadiner[7], Fuchsschaf[7], Rauhwolliges[7], Pommersches Landschaf[7], Soay[7], Broomfield Corriedale[7]
Dermatofilose	Bovino - N'Dama[5], Guadalupe Creole[5]
Leucosis	Bovino - Crioulo Colombiano[8], Harton del Valle[9], Bestuzhevskaya[7], Krasnaya Gorbatovskaya[7], Istobenskaya[7], Kholmogorskaya[7], Suksunskaya Skot[7], Yakutskii Skot[7], Yaroslavskaya[7], Yurinskaya[7], Sura de Stepa[7]
Foot-and-mouth disease	Bovino - Blanco Orejinegro[10], Curraleiro Pé-Duro[7]
Maedi Visnae	Ovino - Red Maasai[5]
Rift valley fever	Ovino - Red Maasai[5]
Scrapie	Ovino – Wensleydale[5]
Ticks	Bovinos - N'Dama[11,12,13], Crioulo Lageano[14], Brahman[5] Nguni[7], Angoni, Sul Do Save[7], Pedi[7], Bonsmara[7], Shangaan, Kashibi[7], Tswana[7], Pesisir[7], Limousin[7], Javanese Zebu[7], Thai[7], Zebu of Azerbaijan[7], Romosinuano[7], Australian Friesian Sahiwal[7], Australian Milking Zebu[7], Australian Sahiwal[7] Ovino – Nguni[7], Landim[7] Búfalo – Thai[7]
Dermatobia hominis	Bovino - Crioulo Lageano[14]
Unspecific ticks transmitted desease	Bovino – Baoulé[7], Ghana Shorthorn[7], Angoni[7], Brahman[5],
Anaplasmose	Bovino – Cinisara[7], Modicana[7]
Babesiose	Bovino - N'Dama[7], Noire Pie de Meknès[7], Modicana[7], Bos indicus[15,16]
Cowdriosis/Erliquiose	Bovino - N'Dama[5] Ovino – Djallonke[5], West Africa Dwarf[5], Damara[7]
Teileriose	Bovino – Sahiwal[5,17], Small East African Zebu[5] Búfalo – Várias[5]
Tripanosomiasis	Bovino - N'Dama[7,18], Ghana Shorthorn[7,18], Baoulé[7], Lagune[7], Bourgou[7], Muturu[7], Dahomey[7], Somba[7], Namchi[7], Kapsiki Kuri[7], Toupouri[7], Keteku[7], Sheko[7], Jiddu[7], Orma Boran[5] Ovino – Djallonke[5,7,18], Vogan[7], West African Dwarf[5,7], Kirdimi[7] Caprino – Djallonke[7,18], West African Dwarf[5,7], Kirdimi[7], Diougry[7]
Endoparasite	Bovino - N'Dama[5], Madagascar Zebu[7], Javanese Zebu[7] Ovino - Crioula Lanada[19,20], Santa Inês[19,20], Madgascar[7], Kumumawa[7], Garut[7], Malin[7], Priangan[7], Churra Lebrijana (fasciolose)[7], Criollo (vários) [7], Criollo Mora[7], Morada Nova[7], Rahmani[7], Thin Tailed[5,21], Red Maasai[5], Barbados Blackbelly[6], Garole[5], Florida Native[5], Djallonke[5], West African Dwarf[5] Caprino - Yei Goat[7], Small East African[5], West African Dwarf[5] Búfalo - Papua New Guinea[7], Kerbau-Kalang (fasciolose)[7], Kerbau Indonesia (fasciolose)[7]

Source: [1]Maggioli et al. (2013), [2]Vásquez-Flores et al. (2006), [3]Ameni et al. (2007), [4]Martínez et al. (2008), [5]Gibson et al. (2002), [6]Saldarriaga et al. (2000), [7]FAO (2010), [8]Hernández et al. (2011), [9]Hernández et al. (2014), [10]Rodríguez & Ariza (2006), [11]Claxton & Leperre (1991), [12]Mattioli et al. (1993), [13]Mattioli et al. (1995), [14]Cardoso et al. (2014), [15]Kessler & Schenk (1998), [16]Bock et al. (1997), [17]Glass & Jensen (2007), [18]Agyemang et al. (1997), [19]Amarante et al. (2004), [20]Bricarello et al. (2004), [21]Roberts et al. (1997).

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