

Research lines on ruminant resistance to parasites and main results obtained at Embrapa Pecuária Sudeste, São Carlos, SP

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One of the main problems of the animal production in the tropical regions is the presence of ecto and endoparasites. Losses due to gastrointestinal nematodes are estimated to be about 68 million dollars a year (SOUTELLO et al., 2002), while the cost of ticks and tick-borne diseases is between US\$ 13.9 and US\$18 billion annually (DE CASTRO, 1997). In Brazil, special interests can be found in some species as *Haemonchus* spp. and *Cooperia* spp. that are the most prevalent nematodes (BIANCHIN et al., 2007; OLIVEIRA et al., 2009) and in the *Rhipicephalus (Boophilus) microplus* tick and the tick borne diseases.

Brazilian cattle breeds are generally considered resistant to many parasites and to heat tolerance. The main focus of the studies at Embrapa Southeastern Region Animal Husbandry has been bovines, especially from the subspecies *Bos indicus*, since this is a known model of adaptation to tropical environment, and their crosses to *Bos taurus*. Exploring cattle resistance can be an alternative to the producers to reduce the pesticides utilization, which generally increases the parasite resistance and the presence of chemical residues in meat, milk and the environment (GRAF et al., 2004; CASTRO-JANER et al., 2010). The selection of chemical resistant parasites, the increased public demand for residue free animal products and the spreading of parasites to new areas as a possible consequence of global warming are concerns for the management of parasites.

In this way, research with different genetics groups is being developed at Embrapa Southeastern Region Animal Husbandry, aiming to better understand the genetic mechanisms involved in host response to parasites and, among these mechanisms, to identify the ones implicated in the variation for host resistance or resilience. It is known that resistant animals respond differentially to ecto and endoparasites, displaying particular mechanisms, as immune response, cytokines Th1/Th2 polarization, primary and adaptative responses. Parasites stimulate host immune responses by protein and other immunogenic molecules present in almost every life stages (LIEW, 2002) but can evade the host response, and complete its life cycle.

Several research projects on molecular markers and gene expression were conducted by the Embrapa's team aiming to describe the molecular basis of host resistance to tick. For a detailed review see Regitano & Prayaga (2010). In these studies it was demonstrated that bovine resistance to ticks can be attributed to genetic variants on candidate genes and to quantitative trait loci (QTL), fitting a multiloci inheritance model, with few detectable QTLs explaining a small proportion of the genetic variation, the predominance of non-additive effects and a strong genotype-environment interaction.

The utilization of real-time PCR, as a quantitative method, has helped to understand many host – parasite relationships. Expression profiles of genes related to immune response in bovines infected by endoparasites (ZAROS et al., 2007; BRICARELLO et al., 2008) and ectoparasites (PIPER et al., 2008; REGITANO et al., 2008) were described. These works agree that real-time PCR had significantly extended the use of RT-PCR assays, to obtain sensitive, rapid and reliable results in the detection and quantification of cytokine mRNAs.

Differences in gene expression were investigated in both early and late responses to infestation. In a study of first challenged Nelore calves with the tick *Rhipicephalus microplus* compared to naive calves, downregulation of interleukin 2 was found (REGITANO et al., 2008). By comparing the candidate gene expression profile of resistant and susceptible cows, belonging to different purebred and crossbred genetic groups, it has been demonstrated that differential expression between resistant and susceptible groups are breed-specific (REGITANO et al., 2008).

Another strategy of gene expression analysis is the microarray technique. Studying skin microarray mRNA profile of crossbred Senepol x Nelore, Angus x Nelore and purebred Nelore before and after successive infestations with *R. microplus*, Ibelli et al. (2010a) found 1,502 differentially expressed genes. Among the activated genes and pathways activated, chemokins, MAPK and Jak-Stat signaling, cytokine receptors, complement and focal adhesion molecules were the most relevant. In this study, the profiles did not show a genetic group-specific pattern. Besides gene expression, it was possible to show other mechanisms involved in cattle infested with tick, the presence of mast cells in higher number in resistant animals when compared with susceptible genetic groups (IBELLI et al., 2010b), as well as the importance of grooming behavior in this resistant animals (IBELLI et al., 2010c).

Regarding endoparasites, *Haemonchus* spp. are responsible for many losses in animal production and few studies are available to understand this relationship in bovine, especially in zebu cattle. To describe the onset of the response to the first contact of *Bos indicus* with *Haemonchus placei*, mRNA differences of immune response genes were investigated in naive Nelore calves infected and non-infected with this parasite by Ibelli et al. (2011). A strong up-regulation of the interleukine IL-13 was found in both abomasum and abomasal lymphnodes, indicating this cytokine could be acting as a precursor of IL-4, stimulating its increase and probably the protective response in the early infection stage in Nelore cattle. Among the other studied cytokines, TNF- α was about eight times higher in lymphnodes and four-fold less expressed in the abomasal mucosa when comparing infected to the uninfected animals. The contrasting pattern of mRNA levels for this cytokine in both tissues could be a result of local immune modulation exerted by the presence of parasite larvae, since TNF- α was implicated in potentialization of parasite expulsion exerted by IL-13, conferring protection to the host (ARTIS et al., 1999).

From the exposed, one can conclude that molecular genetic studies focusing ruminant host resistance to parasites brought light to some of the mechanisms involved in the bovine response to parasites. This information may be useful for the development of strategies to select resistant animals or to modulate host resistance.

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