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Oral Presentation Session

Transcriptional Profiles of Tick-Infested Skin and Tick Salivary Glands in Contrasting Phenotypes of Tick-Host Interfaces Reveal Patterns that are Associated with Resistance to Ticks.

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Background: Ticks are hematophagous Arachnida. They exert selective pressure on their host's skin, the largest organ of vertebrates, however, little is known about cutaneous effector mechanisms that expel ticks. Bovines present contrasting, heritable levels of resistance to *Rhipicephalus microplus*, the most economically important cattle tick. In order to elucidate the mechanisms that result in these outcomes, we examined the global gene expression profile and the *in vivo* patterns of inflammation of cutaneous reactions to tick bites in indicine and taurine cattle, which are, respectively, resistant and susceptible to ticks. Since tick saliva inhibits host homeostatic responses, we determined the gene expression profiles for salivary glands of nymphs fed on resistant or susceptible bovines.
Methods: Biopsies of skin were made from resistant and susceptible bovines that were naïve or infested with nymphs. Samples from infested animals contained a tick or were non-infested. Gene expression for individual samples was determined with Affymetrix chips. Data was normalized using RMA. Custom packages (RankProd and LIMMA) and a linear mixed model and mixture model fitting approach in "R" were employed to obtain differentially expressed genes. Functional analysis was done using DAVID and Ingenuity packages. Differential counts of leukocytes infiltrating skin were made by means of Giemsa staining. Lymphocytes were phenotyped with specific antibodies. cDNA libraries were constructed with mRNA from salivary glands of nymphs feeding on susceptible or resistant bovines. Inserts of randomly selected clone were sequenced, analyzed and the origin of the ESTs within contigs, whether from ticks fed on susceptible or resistant hosts, was determined (Ribeiro et al., 2006).
Results and Conclusions: The transcriptional profiles from bovine skin revealed that expression of genes encoding Fc receptors, granulysin, tenascins involved in tissue repair, adhesion molecules and chemokines that attract basophils, eosinophils and lymphocytes were significantly up-regulated in resistant hosts. *In vivo* studies showed that cutaneous reactions to ticks in resistant bovines recruited significantly more basophils, eosinophils and T, B, NK and WC1^{+} lymphocytes. In the tick, the most abundantly expressed ESTs formed 22 contigs, all encoding structural, glycine-rich proteins. Furthermore, significantly more of these ESTs were derived

from nymphs fed on susceptible hosts. These glycine-rich proteins were related to keratinocyte envelope proteins, to the PE-PGRS multigene family and to spider silks suggesting a role in tick attachment and disruption of the host's dermis and initiation of adaptive immune responses. *Support: CNPq, FAPESP, ILRI and ICTTD.*

Key words: ticks, skin, inflammation, tick salivary glands, global gene expression profiles, genetic resistance