Identification of genes responsive to *Haemonchus contortus* in sheep

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The presence of gastrointestinal nematodes in sheep production systems throughout the world is a major health problem faced by producers, generating economic losses. The aim of this study was to understand molecular mechanisms underlying host resistance. We compared the abomasal mucosal transcriptome of 17 crossbred ½ Santa Inês and ½ Dorper lambs, previously classified as resistant and susceptible in response to *Haemonchus sp*. infection using RNA-Seq technology. The libraries preparation, genome sequencing and sequence analyses were performed at the Laboratory of Animal Biotechnology - ESALQ, Piracicaba, São Paulo, Brazil. The genome sequencing was processed using the protocol TruSeq RNA Sample Preparation v2 for pair-end reads (Illumina, San Diego, CA, USA). Pooled RNA-Seq libraries were sequenced using an Illumina HiScan SQ sequencer. Raw sequence reads were first checked using FastQC (v0.11.5). The Seqyclean v1.9.7 package was performed to remove sequencing adaptors, low-complexity reads (Phred<24) and reads with length less than 65 base pair. The samples were mapped against the ovine reference genome Oar_v4.0 available at NCBI using Tophat (v2.1.1) software with Bowtie2 (v2.2.9) with default parameters. The uniquely mapped read were used to count against the NCBI annotation Oar_v4.0 for calculating the number of reads per gene using the HTSeq Python (v0.6.1) program. The normalization and identification of differentially expressed genes (DEG) between resistant and susceptible groups were made using DESeq2 package. To correct for multiple hypothesis testing, the Benjamini-Hochberg procedure was used with an FDR of 0.05. Gene Ontology (GO) analysis over differentially expressed genes was performed using DAVID software v6.8. The average of reads per sample before and after filtering was 12.522.573 million and 9.626.457 million, respectively, and the average of mapping rate of filtered reads against to *Ovis aries* Oar_v4.0 reference genome assembly was 79.66%. 36 genes was classified as DEG (FDR < 0.05), which 14 genes was more expressed in the resistant animals and 22 was more expressed in the susceptible lambs. The functional enrichment analysis showed that only the signal term was significantly enriched (Benjamini<0.05). Among the genes present in this pathway, 8 are directly or indirectly related to the immune system. CXCL14, CTLA-4, SLAMF7, DPEP2, dipeptide 3 (LOC101110613) and ICOS were more expressed in susceptible animals while mast cell protease 1A-like genes (LOC101105730) and butyrophilin-like protein 1 (LOC101111058) were more expressed in resistant sheep. Our find suggest that the expression of CTLA-4 acts as a negative regulatory molecule for T cells, making the animals more susceptible to infections by *Haemonchus sp*. In addition, SLAMF7 is also involved in greater susceptibility of sheep to parasites, since this gene directs the immunity to a Th1 response. The other DEGs did not show a pattern according to the resistance and susceptibility profile, different from expected.

Keywords: endoparasites, immune response, RNA-Seq, *Ovis aries*, resistance