UNDERSTANDING INNATE IMMUNE RESPONSES TO DNA VIRUSES USING THE DROSOPHILA MELANOGASTER MODEL

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Background: The fruit fly, Drosophila melanogaster, is a well-characterized animal model to study innate immunity to diverse pathogens, including viruses. In addition, the fly genome is very well annotated which is essential to study differential gene expression and transcriptional responses. Thus, the fruit fly is a good model to characterize the interaction between the host innate immune system and a DNA virus in order to understand diverse aspects of the antiviral response. Methods and Results: In order to understand the host response to virus infection, we infected adult Drosophila with Invertebrate iridescent virus 6 (IIV6), which has a double stranded DNA genome. We extracted RNA from individuals after 6, 12, 24 and 72 hours post infection and constructed libraries that were deep sequenced using the SOLiD platform. Here, we focused our RNA-seq analysis on the reads that mapped to the host genome. Around 8622 Drosophila genes were present at a significant level of expression (>10 FKPM) and 1618 were differentially expressed between the four libraries in pairwise comparisons. These genes showed GO (gene ontology) enrichment for 14 biological processes, out of which, 13 are related to immune response, suggesting that IIV6 infection is a powerful stimulus to the immune system. Considering the expression pattern, these 748 genes were separated in 16 clusters, which were analyzed separately for specific GO-enrichment. 8 out of the 14 clusters showed enrichment for genes involved in immune responses and host defense. The main processes that are related with immune response were: defense response, response to stress, response to other organisms and immune system process. In the clusters that not shown enrichment for immune response the main processes were: locomotion, digestion, ATP biosynthetic process, muscle sínteses, anatomical structure development, structural molecule activity, sex differentiation and cytoplasm organization.In order to understand the co-regulation of gene within each cluster, we extracted the promoter region of all genes in the 8 immune process-enriched clusters and identified the presence of 25 commons transcription factors binding sites. The presence of those transcription factors can help explain the co-expression of those genes in response to IIV6 infection. We are currently investigating the role of pathways and transcription factors that we identified to determine whether they are involved in the antiviral response against IIV6. We are also comparing our results to gene expression signatures induced in response to other pathogens Drosophila in order to define specific signatures activated by a DNA virus. Conclusion: We have successfully validated our Drosophila model to understand how the innate immune system responds to infection by a DNA virus. Ultimately, this model could also help elucidate how the mammalian immune system responds. Financial support: CAPES, CNPq, FAPEMIG and PRPq-UFMG

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