INTRODUCTION: Heme functions as an essential prosthetic group of many proteins and, in mammalian cells, heme also functions as an intracellular regulator of gene expression. Heme-specific cell signaling, though, is poorly described in the literature. Heme-related changes are frequently associated with the iron atom in its structure or its ability to act as a pro-oxidant molecule. During hemoglobin degradation in the gut of hematophagous insects, great amount of free heme is produced, which is capable of promoting oxidative damage and specific cell signalling. However, little is known about the heme/ROS-responsive molecular signaling in these insects. MATERIAL AND METHODS: Using an Aedes aegypti cell line model, Aag2, we performed a comparative genome-wide analysis of the regulation induced by heme or Paraquat (a pro-oxidant molecule), through RNA microarray. The microarray results were validated using qPCR. We also performed DHE superoxide specific quantification by HPLC, lactate production quantification and bacterial growth assays. RESULTS: Most of the commonly regulated genes are involved with redox stress response, cell cycle regulation and cell/mitochondrion metabolism. However, the robust heme-induced changes do not seem to be related to iron neither ROS. Interestingly, immune-related genes are down-regulated in the presence of heme. In fact, heme incubated cells are more susceptible to bacterial and viral (DENV) challenges. Furthermore, the oxidative and heme challenges seem to perform a metabolic shift on energy metabolism in these cells, favoring glycolysis and fermentation. The in vivo model appears to undergo a similar response. When the female mosquitoes are fed with a heme solution, it elicits an antioxidant response and induces the bacterial proliferation in the gut. CONCLUSION: Taken together, our results suggest that A. aegypti cells have the ability to assemble an important adaptive response to heme that has global impact on cell metabolism and immunity.

Keywords: heme, mosquito, ROS, gene expression
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