Heme, Hemozoin, Urate and Their Influence Upon Proliferation and Differentiation of *Trypanosoma cruzi*

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The co-evolution of *T. cruzi* and triatomines has promoted the development of a close interaction based on both vector and parasite mechanisms. Heme is an important molecule in the metabolism of living organisms and we showed that the addition of heme increases *Trypanosoma cruzi* epimastigotes (EPI) proliferation in a dose-response manner (Lara *et al*, 2007). As well as heme other molecules present in the vector, such as hemozoin and urate, could regulate proliferation and differentiation of parasites during its contact to the insect host. Although these molecules are present in high concentration inside the vector, their role in metacyclogenesis has not been ruled out. Then, the aim of this work is to investigate the role of molecules upon *T. cruzi* biology. We analyzed metacyclogenesis according to Contreras *et al* 1985, in the presence of heme, urate (found in the triatomine urine), and hemozoin (heme molecules crystallized into dimmers). Therefore, parasites supernatant were observed for 24, 48, 72, 96 h and the evolutive forms were differentiated according to the position of kinetoplast. At 96h, we observed a decreased of 25% and 22% in total cell number when parasites were treated with heme or hemozoin, respectively, while urate showed a 21% increase when compared to the control. In addition, in all treatments, we found an enrichment of trypomastigotes. We also investigated the effects of urate and hemozoin upon EPI proliferation. Parasites were incubated in the presence of urate or hemozoin for 12 days. Thus, we observed that urate impaired the proliferative effect of heme, while, hemozoin presented no effect upon EPI proliferation. Hence, our data suggest that hemozoin, a byproduct of the vector blood digestion, is not implicated in the proliferation and decreases differentiation rates. Differently, urate found in the insect urine, stimulates metacyclogenesis, oppositely, heme, a molecule highly related to proliferation, decreases differentiation, suggesting a novel range of molecules present in the digestive tract modulating parasites multiplication and differentiation. Supported by FAPERJ