INVOLVEMENT OF CAMKII IN PROLIFERATIVE EFFECT OF HEME (FE-PROTOPORPHYIRIN IX) IN *Trypanosoma cruzi*

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Trypanosoma cruzi, the ethiologic agent of Chagas disease, is transmitted through triatomine vectors during their blood-meal on vertebrate host. Since *T. cruzi* epimastigotes live in constant presence of heme, we have investigated the role of heme at cell proliferation as a signaling molecule. We evaluated the effect of several PK inhibitors *in vitro.* Among all inhibitors tested, only KN-93, inhibitor of CaM kinases, had a signifficative effect at cell proliferation mediated by heme. When KN-92, an inactive analogue, was tested there was not effect, confirming the specificity of KN-93. In order to identify the CaMK involved, we tested the peptide Myr-AIP, a highly specific inhibitor derived from the CaMKII substrate. We observed the addition of inhibitor blocked the parasite growth in the presence of heme, confirming the involvement of CaMKII pathway. We showed the increase of CaMKII phosphorylation in the presence of heme, through western blotting, confirming the presence of CaMKII in this process. Subsequently, we assayed this activity using a recombinant commercial enzyme. The addition of heme in the medium for measuring the enzyme activity enhanced up to 10-fold, corroborating the others results and suggesting binding sites for heme in CaMKII.
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