Calcium entry in Trypanosoma brucei is regulated by phospholipase A2 and arachidonic acid

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Abstract

In contrast with mammalian cells, little is known about the control of Ca2+ entry into primitive protozoans. Here we report that Ca2+ influx in pathogenic Trypanosoma brucei can be regulated by phospholipase A2 (PLA2) and the subsequent release of arachidonic acid (AA). Several PLA2 inhibitors blocked Ca2+ entry; 3-(4-octadecyl)-benzoylacrylic acid (OBAA; IC50 0.4+/-0.1 microM) was the most potent. We identified in live trypanosomes PLA2 activity that was sensitive to OBAA and could be stimulated by Ca2+, suggesting the presence of positive feedback control. The cell-associated PLA2 activity was able to release [14C]AA from labelled phospholipid substrates. Exogenous AA (5-50 microM) also initiated Ca2+ entry in a manner that was inhibited by the Ca2+ antagonist La3+ (100 microM). Ca2+ entry did not depend on AA metabolism or protein kinase activation. The cell response was specific for AA, and fatty acids with greater saturation than tetraeicosanoic acid (AA) or with chain lengths less than C20 exhibited greatly diminished ability to initiate Ca2+ influx. Myristate and palmitate inhibited PLA2 activity and also inhibited Ca2+ influx. Overall, these results demonstrate that Ca2+ entry into T. brucei can result from phospholipid hydrolysis and the release of eicosanoic acids