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Could Macropinocytosis Be a New *Trypanosoma cruzi*'s Entry Pathway into Peritoneal Macrophages?

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Several intracellular pathogens are internalized by host cells via multiple endocytic pathways. It is not different with *Trypanosoma cruzi*, the ethiological agent of Chagas disease. *T. cruzi* presents a complex life cycle, involving several developmental stages found in the vertebrate and the invertebrate hosts. In vertebrate host, the metacyclic trypomastigotes invade cells found in the inoculation site through several mechanisms. Evidences indicate that *T.cruzi* entry may occur by endocytosis/phagocytosis or by an active manner. Although macropinocytosis was considered as an endocitic process where cells internalize only large amounts of solutes, several pathogens entry in host cell by this pathway. Our previous results showed that trypomastigotes can entry into peritoneal macrophages in macropinosome-like structures. To investigate if a macropinocytosis-like process would take place in *T. cruzi* entry, a selective macropinocytosis and membrane ruffling inhibitor was used. When pre-treated peritoneal macrophages with amiloride were allowed to interact with *T.cruzi,* we observed a drastic reduction in the entry process of all developmental forms. By field emission scanning electron microscopy, we observed that parasites remained only attached to the host cell plasma membrane. Trypomastigotes and epimastigotes presented part of their bodies recovered by a large part of host cell plasma membrane after two hours of infection. This process, when observed in control experiments, showed, in the most part of interaction events, parasites covered by a cup-like structure originated from macrophage plasma membrane until they are completely internalized. By transmission electron microscopy we observed that internalized parasites were found in the cell periphery. Proteins like Rabankirin 5, tyrosine kinase protein and PI3 kinase, which participate of macropinososme formation, were localized in *Trypanosoma cruzi*'s entry sites. We also observed a colocalization between the parasite and the endocytic fluid phase markers. Together, these results suggest that *T.cruzi* can also entry into peritoneal macrophages using the macropinocytosis pathway.

Keywords: Trypanosoma cruzi, macropinocytosis, peritoneal macrophage