Chip-calorimetric assessment of heat generation during Ca^{2+} uptake by digitonin-permeabilized *Trypanosoma cruzi*

M. R. Sartori[1], J. Lerchner[2], R. F. Castilho[1], P. O. Volpe[3], F. Mertens[2], A. E. Vercesi[1]

[1]Department of Pathology, Faculty of Medical Sciences, University of Campinas (UNICAMP), Campinas, SP 13083-887, Brazil

[2]Institute of Physical Chemistry, TU Bergakademie Freiberg, Leipziger Str. 29, 09599 Freiberg, Germany

[3]Institute of Chemistry, University of Campinas (UNICAMP), Campinas, SP 13083-861, Brazil

Ca^{2+} signaling in trypanosomatids is an important component of energy metabolism regulation and therefore, cytosolic Ca^{2+} concentration is finely regulated by Ca^{2+} transport through the plasma membrane and Ca^{2+} uptake and release by intracellular organelles. To maintain intracellular Ca^{2+} homeostasis with different gradients of the ion within the cellular compartments, there is an energy cost and also energy dissipation in the form of heat. Using an innovative segmented fusion technique of a chip-calorimeter [1] and CRISPR/Cas9 knockout (-KO) *Trypanosoma cruzi* cell lines, we evaluated the heat generation during Ca^{2+} uptake by digitonin-permeabilized *T. cruzi* epimastigotes, a system consisting of Ca^{2+} uptake predominantly by mitochondria and acidocalcisomes. We used three *T. cruzi* epimastigotes cell lines: control cells denominated scrambled, cells with the absence of the pyruvate dehydrogenase phosphatase (*TcPDP*-KO) and cells lacking mitochondrial Ca^{2+} uptake via the mitochondrial calcium uniporter (*TcMCU*-KO), that presented, in this respective order, decreasing rates and capacities of Ca^{2+} uptake. *TcPDP*-KO cells exhibited the lowest heat production following Ca^{2+} addition, which may be due to its lower mitochondrial oxidative phosphorylation capacity and lower ATP availability for acidocalcisomal Ca^{2+} uptake. Scrambled and *TcMCU*-KO cells exhibited similar Ca^{2+}-induced heat effects, which correlates with a higher ATP-dependent acidocalcisomal Ca^{2+} uptake in these cells. Our results show evidences that mitochondrial Ca^{2+} transport via the uniporter is minimally heat dissipative while ATPase pumps in acidocalcisomes possess a predominant contribution to the heat generated during Ca^{2+} uptake.

Keywords: *Trypanosoma cruzi*, Calcium signaling, Calcium transport, Energy metabolism, Chip calorimetry, Heat production

[1] Lerchner J, Sartori MR, Volpe PO, Förster S, Mazik M, Vercesi AE, Mertens F. Segment fusion chip calorimetry: a new method for the investigation of fast reactions. J Therm Anal Calorim. 2021; Available from: https://doi.org/10.1007/s10973-021-10623-7