THE MITOCHONDRIAL PLASTICITY IN CHAGAS DISEASE

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Chagas disease (CD) is caused by the protozoan Tryoanosoma cruzi. Currently 8 million people are infected, mainly at Latin America (Endemic area). Only benznidazole and nifurtimox are avaliable to treat CD, but they are partially effective in the acute phase and ineffective in the chronic phase of the disease. Based on this, new targets and therapies are needed.

Host mitochondria are affected in different phases of CD. Increased mitochondrial density and size were reported after T. cruzi infection. These alterations follow the parasite proliferation and parasite-host mitochondria co-localization. However, the real contribution of host cell mitochondria, during infection and tissue degeneration caused by CD are not know. Considering that mitochondria are extremelly dynamic and plastic, capable of change their number, size and density, based on tissue metabolic demand, we hypothesized that the parasite infection and the tissue degeneration depends on host cell mitochondria morphological reorganization and function. Also, the modulation of these process can control and/or prevent the parasite infection and/or CD progression. This way, the aim of this project is investigate the role of mitochondrial plasticity of host cell during T. cruzi infection and tissue degeneration. For this, we used the immortalized lineage of mouse embryonic fibroblast (MEF) WT and knockout (Mfn1, Mfn2, Mfn1 / 2, Opa1, Fis1, Mff and Atg5) infected with *T. cruzi* (CL-14). After 3h post infection an increased percentage of infected cells were observed in Mfn2, Mfn1 /2, Opa1 and Fis1, compared to WT. No difference were noted between WT cells and Mfn1, Mff and Atg5 knockout cells. Using human hearts samples were observed an reduced Citocrome C oxidase expression and increased p62 and Beclin-1 expression, when compared the chagasic heart with the health control heart, which indicates mitochondrial dysfunction and increase or inefficiency autophagic flux during Chagas disease. These data point to a mitochondrial dysfunction during Chagas disease. And suggest that the absence of proteins related to mitochondrial fusion and fission aggravates the parasite infection.