Dual and Opposite Roles of Reactive Oxygen Species (ROS) in Chagas Disease: Beneficial on the Pathogen and Harmful on the Host

Maldonado, E.
Rojas, D.A.
Morales, S.
Miralles, V.
Solari, A.

Abstract
Chagas disease is a neglected tropical disease, which affects an estimate of 6-7 million people worldwide. Chagas disease is caused by Trypanosoma cruzi, which is a eukaryotic flagellate unicellular organism. At the primary infection sites, these parasites are phagocytized by macrophages, which produce reactive oxygen species (ROS) in response to the infection with T. cruzi. The ROS produce damage to the host tissues; however, macrophage-produced ROS is also used as a signal for T. cruzi proliferation. At the later stages of infection, mitochondrial ROS is produced by the infected cardiomyocytes that contribute to the oxidative damage, which persists at the chronic stage of the disease. The oxidative damage leads to a functional impairment of the heart. In this review article, we will discuss the mechanisms by which T. cruzi is able to deal with the oxidative stress and how this helps the parasite growth at the acute phase of infection and how the oxidative stress affects the cardiomyopathy at the chronic stage of the Chagas disease. We will describe the mechanisms used by the parasite to deal with ROS and reactive nitrogen species (RNS) through the trypanothione and the mechanisms used to repair the damaged DNA. Also, a description of the events produced by ROS at the acute and chronic stages of the disease is presented. Lastly, we discuss the benefits of ROS for T. cruzi growth and proliferation and the possible mechanisms involved in this phenomenon. Hypothesis is put forward to explain the molecular mechanisms by which ROS triggers parasite growth and proliferation and how ROS is able to produce a long persisting damage on cardiomyocytes even in the absence of the parasite.

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