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ASSIGNMENT

High metabolic activity of some protozoa pathogen results in the high production of reactive oxygen intermediate. How is this possible?

Reactive oxygen intermediates such as Reactive Oxygen Species (ROS) are used by the immune system as weapons against pathogens. They are deadly weapons used by phagocytes and other cell types, such as lung epithelial cells, against pathogens. ROS can kill pathogens directly by causing oxidative damage to biocompounds or indirectly by stimulating pathogen elimination by various nonoxidative mechanisms, including pattern recognition receptors signaling, autophagy, neutrophil extracellular trap formation, and T-lymphocyte responses.; however, antioxidants have long been recognized as protectors of host organism against infections. This brings about a paradox since the inhibition of ROS by antioxidants promotes infection. It is plausible that the paradox contained in these statements can be solved by the failure of antioxidants to neutralize the ROS involved in pathogen killing (*e.g.*, by not reaching the appropriate location required to their action) and by the capacity of antioxidants to protect immune cells from the damage caused by ROS. The nature of the microbes and their susceptibility to ROS can also offer a clue to solve the paradox. ROS effectively combat certain microbes, whereas other microbes seem to thrive in oxidative environments.

ROS can promote pathogen elimination by direct oxidative damage or by a variety of innate and adaptive mechanisms. When a microbe is recognized by phagocytes and engulfed, it triggers a process, named respiratory burst, in which phagocytes elevate their oxygen consumption. The enzyme NADPH-oxidase (NOX2) is pivotal to the respiratory burst and attaches to the phagosomal membrane during phagocytosis. Particular stimuli such as phorbol-12-myristate-13-acetate (PMA) stimulation can promote NOX2 attachment to the cell membrane. NOX2-derived ROS promote oxidative and nonoxidative mechanisms of microbe elimination.

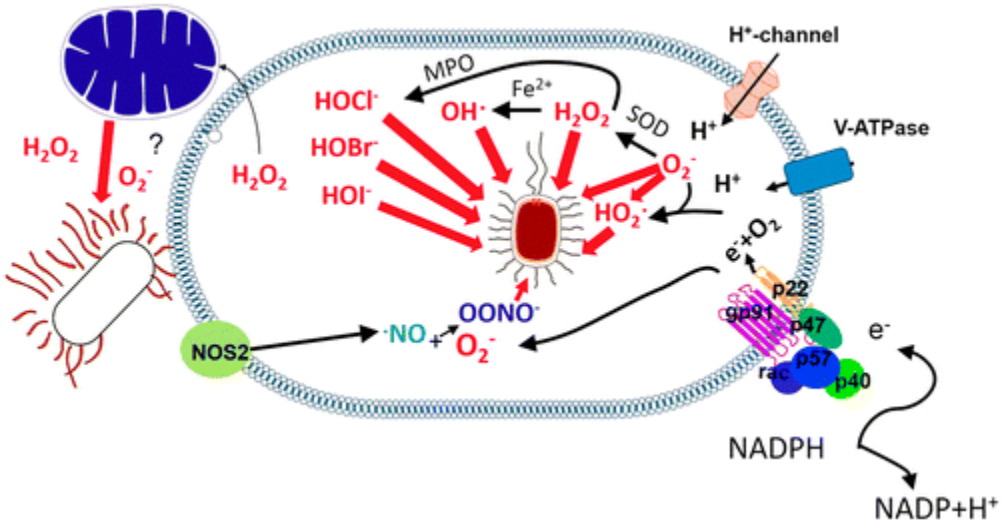

Fig 1: Various ROS produced within the phagosome cause oxidative damage (red *arrow*) to phagocytosed pathogens.

ROS can also affect pathogens indirectly by activating pro-inflammatory cytokines which makes the environment unfavorable for the pathogens. ROS can also initiate apoptosis of host cell which concomitantly takes down the pathogen. Since **metabolism** is a set of complex chemical reactions used to sustain life. The protozoa pathogen will naturally use its metabolic activities to sustain its life in the host cell. This triggers the production of ROS by the host cell to eliminate them but this in turn increases the metabolic activity of the pathogen since it wants to continue

thriving in the host cell. This leads to a continuous cycle of high metabolic activity on the part of the protozoa pathogen and the production of ROS on the part of the host until the pathogen is eliminated. Therefore, it can be said that the metabolic activity of the pathogen is proportional to the production of ROS by the host cell.

Several authors have discussed the implications of free radicals through oxidative stress in the physiopathogenesis of malaria (caused by *Plasmodium falciparum*, a protozoa pathogen). This involvement may be related to the pathogenic mechanisms triggered by the parasite, as well as free radical production and antioxidant defenses in host cells to abate the infection. Recent studies suggest that the generation of reactive oxygen and nitrogen species (ROS and RNS) associated with oxidative stress, plays a crucial role in the development of systemic complications caused by malaria. Malaria infection induces the generation of hydroxyl radicals (OH) in the liver, which most probably is the main reason for the induction of oxidative stress and apoptosis.