

Examining the function of the *A. fumigatus* peroxiredoxins in oxidative damage and virulence

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Aspergillus fumigatus, is a saprophytic filamentous fungus and the most prevalent specie causing *Aspergillus* related human diseases including the invasive pulmonary aspergillosis, the life threatening form of infection. The ability of the pathogen to remain inside the host greatly relies on the functionality of its antioxidant mechanisms which drive the pathogen response against the respiratory burst and Reactive Oxygen Species (ROS) detoxification generated by the host's protective response. Among these protective mechanisms lie a number of antioxidant enzymes such as the superoxide dismutase (SOD), catalase (CAT), glutathione peroxidase (GPx) and peroxiredoxins (Prx). In order to investigate the role played by *A. fumigatus* peroxiredoxins in the ROS tolerance, we characterized the three peroxiredoxins in *A. fumigatus* (*prxA-C*). The *A. fumigatus* wild type and null Prx mutant strains were exposed to the oxidative and cell wall stressing agent as well as to the main drugs used to treat aspergillosis. Only the $\Delta prxB$ (Afu4g08580) mutant strain showed increased sensitivity to paraquat while $\Delta prxA$ (Afu5g15070) and $\Delta prxC$ (Afu8g07130) were as sensitive as the wild-type strain for all the drugs tested. There was no other morphological defect associated to the $\Delta prxA-C$ loss of function. Protein abundance evaluation indicated that the three peroxiredoxins are constitutively expressed regardless of the induction of oxidative damage by hydrogen peroxide (5 mM). PrxB is a cytosolic protein while PrxC is localized in the mitochondria. PrxA presents cytosolic localization but it remains to be determined if it is also located in mitochondria. The $\Delta prxA$ also showed virulence attenuation in a neutropenic mouse model of pulmonary invasive aspergillosis. These results indicate a role for *prxB* in the virulence of *A. fumigatus* but also a redundant function of the peroxiredoxins with other components of the antioxidant system in *A. fumigatus*.

Keywords: *Aspergillus fumigatus*, peroxiredoxin, reactive oxygen species

Financial support: FAPESP