miR-193b Regulates Host Defense Against Leishmania braziliensis by Promoting Reactive Oxygen Species Production

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ABSTRACT

Leishmaniasis is one of the most neglected diseases in the world. Cutaneous leishmaniasis (CL) is the most common form of this disease, characterized by ulcerated skin lesions and chronic inflammation. The underlying mechanisms of its pathogenesis are not fully understood, and little is known about post-transcriptional regulation during CL. In this process, small non-coding RNAs play a crucial role. MicroRNAs (miRNAs) are small endogenous RNAs that modulate expression through translational repression or target RNA degradation. These findings highlight the potential to identify miRNA expression associated with disease prognosis or severity. Previously, we demonstrated that miR-193b, miR-671, and TREM1 show significant correlation only in patients with faster healing (up to 59 days) and not in those requiring longer healing times (over 60 days). These results suggest that this axis may be strongly associated with the healing time of patients with cutaneous leishmaniasis (CL). Therefore, the aim of this study was to investigate the role of miR-193b in macrophages infected with Leishmania braziliensis (Lb). For this, human macrophages were infected with Lb to validate the expression profile of miR-193b in CL at 30 minutes, 4 hours, and 12 hours. Then, the macrophages were transfected with miR-193b and infected by Lb for 4 and 12 hours to evaluate its role in infection control. Additionally, reactive oxygen species (ROS) were assessed in the presence of miR-193b overexpression. The expression profile of miR-193b was significantly inhibited in these cells after 30 minutes and 4 hours of infection; however, this expression was induced at the 12-hour time point. Macrophages transfected with miR-193b after 12 hours of infection, there was a significant reduction in parasitic load and the number of amastigotes per cell. The reactive oxygen species (ROS) assay revealed that miR-193b promoted an increase in ROS in macrophages infected for 12 hours, reforcing the potential of this miRNA in infection control. Conclusion: Taken together,

these analyses show that miR-193b promotes infection control by Lb in human macrophages after 12 hours through the induction of reactive oxygen species leading to a better disease outcome.

KEYWORDS: miR-193b, macrophage, Leishmaniasis.

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