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Topic of Research: "Study of host mi-RNA mediated alteration in the lipid metabolic pathway of macrophages during *Leishmania* infection"

ABSTRACT SUMMARY

Background: Leishmania donovani is the etiological agent of the neglected tropical disease-visceral leishmaniasis. The parasites replicate inside the phagolysosomes or the parasitophorous vacuoles of the host macrophages and dendritic cells, known as antigen presenting cells (APCs). The infected macrophages show decrease in host cellular cholesterol level leading to increase in membrane fluidity and compromised cellular response.

Methodology/ principal findings: In the present study we observed that Leishmania donovani infection in THP-1 derived macrophages, leads to suppression in the expression of the important cholesterol biosynthetic genes in a time specific manner and parallelly the upregulation of specific miRNAs- hsa-miR-874-3p and hsa-miR-1303. hsa-miR-874-3p seed region have strong 8mer nucleotide complementarity with the 3'UTR of HMGCS1 and the other cholesterol biosynthetic genes. The hsa-miR-1303 seed region shows strong 8mer complementarity specifically with 3'UTR of rate limiting enzyme HMGCR. By suppressing the expression of these upregulated miRNAs, with the help their respective miRNAs antagomir, the expression of their predicted target was upregulated as compared to the infected macrophages, and subsequently there was significant decrease in the intracellular parasite count was observable. In addition, we found that, respective miRNA mimic transfection results in the decrease in the expression of the target mRNA.

Conclusions: This study demonstrates the miRNAs, that can putatively play important role the regulation of the expression of different cholesterol biosynthetic genes. Identification of the miRNA- hsa-miR-874-3p, which regulate the expression of HMGCS1 and has-miR-1303 which regulate the expression of HMGCR during L. donovani infection. These noble findings provide a new platform for the development of new therapeutic option against leishmaniasis.