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Exploring the Role of Immune-Modulators in Pathogen Recognition Receptor NOD2 Mediated Protection against Visceral Leishmaniasis

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Abstract : Background: Leishmania donovani infection causes severe host immune-suppression through the modulation of pathogen recognition receptors. Apart from TLRs (Toll Like Receptor), recent studies focus on the important contribution of NLR (NOD-Like Receptor) family member NOD1 and NOD2 as these receptors are capable of triggering host innate immunity. The aim of this study was to decipher the role of NOD1/NOD2 receptors during experimental visceral leishmaniasis (VL) and the important link between host failure and parasite evasion strategy. Method: The status of NOD1 and NOD2 receptors were analysed in uninfected and infected cells through western blotting and RT-PCR. The active contributions of these receptors in reducing parasite burden were confirmed by siRNA mediated silencing, and over-expression studies and the parasite numbers were calculated through microscopic examination of the Giemsa-stained slides. In-vivo studies were done by using non-toxic dose of Mw (Mycobacterium indicus pranii), Ara-LAM(Arabinoasylated lipoarabinomannan) along with MDP (Muramyl dipeptide) administration. Result: Leishmania donovani infection of the macrophages reduced the expression of NOD2 receptors whereas NOD1 remain unaffected. MDP, a NOD2-ligand, treatment during over-expression of NOD2, reduced the parasite burden effectively which was associated with increased pro-inflammatory cytokine generation and NO production. In experimental mouse model, Ara-LAM treatment increased the expression of NOD2 and in combination with MDP it showed active therapeutic potential against VL and found to be more effective than Mw which was already reported to be involved in NOD2 modulation. Conclusion: This work explores the essential contribution of NOD2 during experimental VL and mechanistic understanding of Ara-LAM + MDP combination therapy to work against this disease and highlighted NOD2 as an essential therapeutic target.

Keywords : Ara-LAM (Arabinoacylated Lipoarabinomannan), NOD2 (nucleotide binding oligomerization receptor 2), MDP (muramyl di peptide), visceral Leishmaniasis
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