Nikhil Chauhan et al., J Bacteriol Parasitol 2017, 8:3 (Suppl)
DOI: 10.4172/2155-9597-C1-031

Molecular, Functional and Immunological Characterization of Macrophage Migration Inhibitory Factor-2 of Human Lymphatic Filarial Parasite *Wuchereria bancrofti*

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Helminthes are notorious for modulating host immune responses that help them survive for several years in the hostile environment in the host and cause the disease process. Several studies were conducted in the past one decade to identify how the parasites were able to achieve this. It was demonstrated that the helminth parasites are capable of producing molecules that can suppress or deviate host immune responses targeted against them. Macrophage Migration Inhibitory Factor-2 (*MIF-2*) is one such molecule produced by filarial parasites that is believed to have significant immunomodulatory function on host macrophages and monocytes. In this study we cloned and characterized *MIF-2* from *Wucheraria bancrofti*. *Wba-mif-2* cDNA (363 bp) were amplified from λZAP cDNA library of *W. bancrofti* third stage infective larvae and cloned into the pRSETB expression vector. The annotation of *Wba-mif-2* gene showed the presence of two exons of 183 bp and 180 bp interspersed with long intron of 3,912 bp (Accession no. BK008885). In an attempt to characterize the function of r*Wba-MIF-2*, we used three known inhibitors of human MIF tautomerase activity. Our studies showed that the r*Wba-MIF-2* tautomerase activity was significantly inhibited by curcumin (58.98%), ISO-1 (50.32%) and 4-IPP (29.17%). Compared to human *MIF-2*, the signature C57XXC60 catalytic site for oxidoreductase activity was found to be absent in r*Wba-MIF-2*. However, homology modeling showed that Cys58 and Cys95 are in close association (at a distance of 3.23 A° with pKa value 9.0) and may function in the oxidoreductase activity. PCR based site directed mutagenesis in Cys58Ser and Cys95Ser of r*Wba-MIF-2* abrogated the tautomerase activity suggesting a vital role for these cysteine residues in the oxidoreductase activity of r*Wba-MIF-2*. Addition of r*Wba-MIF-2* to LPS stimulated RAW 264.7 cells resulted in significant suppression of IL-6 secretion by the macrophages. These findings suggest that r*Wba-MIF-2* has significant immunomodulatory functions capable of downregulating macrophage mediated inflammatory responses.

Biography

Nikhil Chauhan, completed his PhD and working as an research associate at Department of Biomedical Sciences, College of Medicine Rockford, University of Illinois, Rockford, Department of Microbiology & Immunology under the super vision of Dr. Ramaswamy Kalyanasundaram, Professor & Head of Department.

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