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Leishmania recombinant antigen modulates the macrophage effector functions synergizing anti-leishmanial effects of miltefosine to facilitate early clearance of intracellular parasites

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The limited and toxic chemotherapeutic options for Leishmaniasis endorse the need for development of new alternatives. Partial success of anti-leishmanial drugs/vaccines and a fine balance of host-parasite interaction suggest the use of immunomodulators as a rational approach. We evaluated the immunomodulatory/immunotherapeutic properties of Leishmania recombinant antigens (recAg) in terms of macrophage activation and intracellular parasite clearance alone as well as in combination with standard anti-leishmanial drugs, in order to assess the potential use of immunomodulators for early clearance of intracellular parasites along with sub-optimal doses of anti-leishmanial drugs, that way reducing the toxicity also. Percentage of cells producing intracellular NO (14.25+2.76%) and ROS (30.6+3.51%) as assessed by flowcytometry using DAF-2DA and DCF-2DA dyes, were significantly increased among peritoneal macrophages when stimulated with recAg. Treatment of infected macrophages with recAg enhanced their phagocytic (47.00+3.46) as well as killing index (33.97+2.48) that coupled with increased intracellular parasite clearance. The recAg showed synergistic effect with miltefosine causing almost complete clearance of amastigotes at sub-optimal drug dose (10μM) at 48 h and significantly reducing the number of infected cells. A concomitant increase in the production of inflammatory cytokines, IL-6 (3026.38+324.53), TNF-α (357.03+38.34) and MCP-1 (3574.74+784.62) was also observed when infected cells were stimulated with recAg. The leishmania recAg potentiates effector functions of parasitized macrophages and synergises with antileishmanial drug miltefosine in early clearance of parasites at suboptimal drug dose, thus placing it as a promising candidate for adjunct therapy.

Biography

Sunil K Arora completed his PhD in Immunology from Post Graduate Institute of Medical Education & Research, Chandigarh, India in 1987 and did his Post-doctoral fellowship from the Division of Infectious Diseases, Department of Medicine, University of Texas Health Science Center at San Antonio, San Antonio, Texas, USA from 1991-1993. He is currently working as Professor of Immunopathology and Head of Translational & Regenerative Medicine at PGIMER, Chandigarh, India. He has been visiting Professor to King's College London, UK, University of Miami, USA and Hannover Medical School Hannover, Germany. He has published more than 125 research papers in peer reviewed indexed journals of repute, mainly in the area of HIV, Leishmaniasis and HCV.

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