Title: Understanding the immunology of kala-azar for innovations in its elimination and control.

Abstract

Visceral leishmaniasis (VL) is a neglected tropical disease accounting for second highest mortality worldwide, with an estimated 50,000 to 90,000 new cases annually. India alone accounts for 50% of the global VL cases. Considering the growing drug-related toxicities, parasite resistance, HIV-coinfection, the development of an effective vaccine for leishmaniasis remains a global priority. A clear understanding of host immunology and role of T cells in long-lasting memory generation is extremely essential to control hard-to-treat infections like VL. Although human VL is characterized by high *Leishmania*-specific antibodies, inadequate/ depressed CMI response and lack of protective cytokines are hallmarks of disease progression. Evident from our clinical studies, both $CD4^+$ and $CD8^+$ T cell-mediated IFN-gamma and IL-12 production with concomitant down-regulation of IL-10, TGF-β and IL-35 may eventually lead to successful cure. Further, the life-long immunity against re-infection and relatively simple life-cycle of *Leishmania* parasites show feasibility of vaccine development against this disease. Poor immunogenicity and failure to generate lasting protection are the major obstacles of subunit vaccines against leishmaniases. I would address our continuous efforts to develop DNA and protein-based vaccine candidates to confer desired Th1-biased $CD4^+$ and $CD8^+$ T cell response in preclinical models. Formulations of the liposomal vaccines with other potent adjuvants can promote long-term immunological memory when delivered via human administrable routes. In order to minimize the drug-related toxicities, we have also developed liposomal drug formulations for single-shot therapy, providing dual protection by its antileishmanial and immunomodulatory functions at lower doses.

Secondly, in order to alleviate the drawbacks of conventional invasive VL diagnostic methods, we have validated the non-invasive, rapid serum and urine-based ELISA and dipstick assays for successful diagnosis of this disease.