Leishmaniasis encompasses a group of infectious diseases caused by trypanosomatic protozoa of the genus *Leishmania* and transmitted by Phlebotomine sandfly vectors. These diseases have a worldwide distribution with a clinical spectrum ranging from cutaneous and mucocutaneous lesion, to fatal visceral disease. The fact that cured patients are refractory to re-infection suggests that vaccination against leishmaniasis might be feasible using conventional immunization methods. A cornerstone in the process of vaccine development is the utilization of suitable animal models. The development of non-human primate model for leishmaniasis, which largely mimic the human situation, is therefore desirable for safety and efficacy trials of promising vaccines preceding clinical trials in humans.

The current study was aimed at characterizing protective immunological responses required for *Leishmania* vaccine evaluation in vervet monkey (*Cercopithecus aethiops*) disease model. Specifically, the study addressed the following aspects of leishmaniasis; prevalence of leishmaniasis in a sample of wild caught monkeys, the natural history of *L. major* in vervet monkeys, the bioactivity of recombinant human (rh) IL-12 in vervet monkeys, the cross-reactivity of the Iranian isolate of *L. major* (vaccine antigen: ALM) and Kenyan isolate of *L. Major* (challenge parasite: NLB-144) and the safety and adjuvant potential of recombinant human (rh) IL-12 for a *Leishmania* vaccine in vervet monkeys. Monkeys were sampled by trapping from different parts of Kenya and screened for anti-*Leishmania* specific immunoglobulin G (IgG) by ELISA and for *Leishmania* specific memory T-cells by blast assay.

For the natural history of *L. major* in vervet monkeys, a group of twelve monkeys of which six were *Leishmania* exposed and six were *Leishmania* naive were challenged with *L. major* promastigotes. Disease development was correlated with immunological profiles. The biological activity of rh IL-12 in monkey peripheral blood leucocytes (PBL) and the cross-reactivity between ALM and NLB-144 was established in recall proliferative and IFN-γ responses. For the vaccine trial, five groups of eight monkeys each were vaccinated three times, three weeks apart with either ALM + IL-12, ALM alone or rh IL-12 alone. The other two groups, *L. major* cured and *Leishmania* naive monkeys comprised positive and negative controls respectively. Immunological responses were determined three weeks after the last vaccination. The monkeys were then challenged and immunization-induced protection assessed.

A prevalence of 3.5% of *Leishmania* exposure was established in the wild monkeys (2 out of 59 monkeys). There was a positive correlation between cutaneous disease establishment and immunological profiles. Recombinant human IL-12 was found to be biologically active in monkey cells and high cross-reactivity was found between challenge parasite and vaccine antigen. No untoward side effects of rh IL-12 was noted and vaccination was successful since a strong Th 1 response was observed following immunization. Of all the parameters considered IFN-γ was the most indicative of immunization. Previous vaccine development studies have focused on inducing CD4+ Th 1 responses, however results presented here suggest that other factors could be important for protective immunity. It is also possible that disease-induced immunological responses are different from immunization-induced responses in ways we do not yet understand.