

This thesis is a follow up on my MSc work, which suggested that the LPG was an excellent candidate as a transmission blocking vaccine against *L. major* infections. Previous attempts to vaccinate

BALB/c mice using *L. major*-derived LPG have also been successful against *L. major*.

Therefore, in order to determine whether such results could be extrapolated to visceral leishmaniasis caused by *L. donovani*, susceptible BALB/c mice and Syrian golden hamsters (*Mesocricetus auratus*) were vaccinated with *L. donovani*-derived LPG plus BCG as an adjuvant.

Following a triple vaccination with a total dose of 60µg and 30 µg of LPG for hamsters and BALB/c mice respectively, there were no noticeable side effects both locally and systemically, implying that the molecule was safe at this dosage level. There was an activation of both the humoral as well as cell-mediated responses to LPG mixed with BCG, which correlated with resistance against the disease. Protection by LPG was however; poor as the remaining immunized animals showed disease progression leading to severity of the disease as illustrated by emaciation, weight loss and heavy splenic parasitaemia in hamsters. Furthermore, animals previously immunized with *L. donovani*-derived LPG did not confer protection to *L. major* infections.

Secondly, this study also investigated the effect of monoclonal antibodies (MABs) raised against *L. major*-derived LPG on the development of *L. major in vitro* and in its natural vector *P. duboscqi* Neveu Lemaire (Diptera: Psychodidae). Interestingly, at 36 hours parasites which had previously been incubated together with a 1:100 MABs showed a significantly a high number of early log phase procyclic metacyclic promastigotes ($p < 0.05$). Sand flies, which fed on *L. major* amastigotes mixed with a 1:100 MABs, also showed mainly the procyclics and a few haptomonads on day 6 post-feeding ($p < 0.05$). In the control group, parasite development followed the normal development pattern up to the metacyclic stage. Results also showed that flies, which had fed on anti-*L. major*-derived LPG MABs, showed significantly lower parasitemia levels of less than 3+, compared to their controls which showed parasitemia levels of 4+ ($p < 0.5$). These findings suggest that MABs were effective in reducing sand fly infections and a possible role humoral mechanisms in protection against leishmaniasis.

Finally, this study using SDS-PAGE technique, sought to determine whether the sand fly and the *Leishmania* parasite have molecules with similar molecular weights or not. Interestingly, the sand fly gut lysates and proteins present in *L. major*-derived LPG showed two common molecules of 105kDa and 106kDa respectively. However, anti-LPG MABs did not recognize these sand fly molecules on western blot analysis. Results suggest that further analysis of these individual proteins from the gut should be undertaken with a view of determining their vaccine potential