

8. Summary:

This work can be summarized as:

1. Virulent and avirulent strains show differential expression of leishmanial genes post-infection of primary macrophages. NAD⁺ synthase, LmjF_36_3850, adenylate kinase, TDR1, PAP, LmjF_33_2620 were significantly down-regulated in avirulent strains while HGPRT, Pyruvate kinase and ARP 2/3 complex 16kDa subunit were expressed higher in avirulent strains as compared to virulent *L. major* forms.
2. DNA vaccination with LmjF_36_3850 elicits higher anti-leishmanial IgG2a and IgG1, but produces an overall mixed Th response. Lesion progression in vaccinated mice was comparable to controls. Moreover, parasite burden in draining lymph node was higher in DNA vaccinated mice as compared to control groups. IgG2a and IgG1 levels remained higher even 5 weeks post challenge infection. DNA vaccinated mice had higher population of IgG1 and IgG1 secreting B cells.
3. Lymphocytes from LmjF_36_3850-DNA vaccinated mice had higher expression levels of anti-inflammatory cytokines like IL-4 and IL-10 and co-inhibitory molecules like CTLA-4. Also, vaccinated mice have higher population of Th2-, Th17- and Trg- T_{EM} and T_{CM} cells. Thus, DNA vaccination with LmjF_36_3850 was unable to protect mice against *L. major* challenge.
4. Next, we checked efficacy of HPB vaccination strategy in generating a protective immune response via LmAdeK vaccination. HPB vaccinated mice elicited higher levels of IgG2a than IgG1 and skewed response to protective Th1 type.
5. HPB vaccinated mice control lesion progression better than other vaccination strategies and had lower parasitic burden in draining lymph node after five weeks of *L. major*

challenge infection. Also, anti-AdeK IgG2a levels remained significantly higher even after 5 weeks of challenge infection.

6. Lymphocytes from draining lymph node of HPB vaccinated mice had higher expression of IFN- γ , while it had lower expression of Th2 and Treg cytokines IL-4 and IL-10 and co-inhibitory molecule CTLA-4. Also, HPB vaccinated mice had lower repertoire of disease-promoting Th17-, T_{EM}, T_{CM} and Treg-T_{EM} cells and IL-4 secreting Th2- T_{EM} and T_{CM} cells.
7. Thus, we conclude that HPB vaccination strategy is efficacious in controlling *L. major* lesion progression and disease burden than other vaccination strategies.