Summary

Vaccine development against leishmaniasis is a serious concern for decades. Advancement in the technology deciphered the host-parasite immune mechanisms, Gene manipulation like Knock-out, Knock-in, Crisper Cas strategy were adopted, immunological phenomena had advanced understanding but not even a single antigenic candidate of *Leishmania* met with success. Drugs with emerging resistance associated with toxicity, suppression of immune system and high price prompt researchers to adopt a new approach towards *Leishmania* vaccine to make it happen and save neglected poor people against deadly leishmaniasis. To date, so many approaches were used but none of them met with success so far. Some are in the trial but failed during the final stages. These failures give a lesson to design a potent antigenic candidate for leishmania to make it possible. As previously we reported a *Leishmania major* MAPK10 induces protection against experimental cutaneous leishmaniasis in a susceptible BALB/c host. So, In order to test the breadth of protection, we sought to determine whether the gene from *Leishmania major* is able to protect against *L. donovani* infection. It is interesting a single antigen of leishmania protects against both forms of leishmaniasis. Our observations support the hypothesis of a single antigen-directed host-protective immune response. Our study revealed several important observations which are mentioned below:

1. LmjMAPK10 or M10 induces T_H1 response but down-regulates the T_H2 phenotype. Co-culture of macrophages with $CD4^+$T-cell elevates IL-12, IFN-γ, TNF-α but suppresses IL-10 and IL-4.

2. M10 reduces the parasite burden in the infected macrophage T-cell co-culture system.

3. M10 immunization reduces the parasite load in visceral organs predominantly spleen and liver because *L. donovani* infection is related to splenomegaly and hepatomegaly and if left untreated becomes fatal.

4. M10 immunized CSA stimulated splenocytes culture supernatant releases increase in production of IL-12, IFN-γ by reducing IL-10 and IL-4. This observation gives a clue towards cell-mediated antigen-specific immune response.

5. M10 immunized sera reveal an antigen-specific immune response by elevating IgG2a. In contrast, IgG1 and IgM suppressed the following challenge. It suggests M10 immunization induces a humoral response against *L. donovani* infection.

6. As NO is responsible for controlling the replication of parasite inside the macrophage. In a macrophage T-cell co-culture system M10 is related to elevated NO-mediated protection.

7. M10 immunization at gene level also supports the elevation of T_H1 type cytokine by diminishing T_H2 type anti-inflammatory cytokine.

8. M10 immunization helps in the T-cell subset by enhancing the population of T_H1 and T_H17 but suppressing T_H2 and Treg cell population by using a phenotypic and intracellular marker in splenocytes.

9. M10+IL-7 immunized mice lead to a reduction in parasite load in primary homing site spleen and liver respectively.

10. M10+IL7 immunized mice show reduced amastigotes/100 cell in an infected macrophage T-cell coculture system.

11. In an infected macrophage T-cell coculture system, M10+IL-7 culture supernatant release an increase in antiparasitic cytokine IL-12 by decreasing IL-10 followed by elevated NO mediates parasite replication.

12. In M10+IL-7 immunized CSA stimulated splenocytes culture supernatant evokes IL-12 and IFN-γ by decreasing pro-parasitic IL-10 and IL-4 cytokine.

13. In addition, M10+IL-7 immunized sera switch towards IgG2a isotypes by suppressing IgG1 and IgM isotypes.

14. M10+IL-7 immunization enhances the population of $CD4^{+}$T-cell subset by elevating T_H1, T_H17, T_M by suppressing T_H2, and Treg cell population by using a phenotypic and intracellular marker in splenocytes.

These key points that we have observed help in vaccination against *Leishmania donovani* infection by using the M10 antigen from *Leishmania major*.