The protection properties of a novel multi-antigenic and multi-epitopes subunit vaccine with pan-HLA coverage against M. tuberculosis

The design of a sub-unit vaccine candidates (VCs) against intracellular pathogens requires the use of antigenic sequences that can induce highly potent, long lasting and antigen-specific responses in the majority of the target population. While past research sought the best epitopes based on their specific antigenicity, we asked whether specific defined domains, i.e. multi-epitope long peptides (LP), have high densities for CD4+ /CD8+ T and B-cell epitopes. Unpredictably, signal peptide (SP) domains were found to meet this goal (Kovjezin et al 2011, Kovjezin et al 2013). The improved antigenicity of these LP domains relies initially on their known hydrophobic nature but more so on their unique antigen specificity (i.e. the antigen from which they are derived). The superiority of these VCs was initially demonstrated by the high percentage of diverse identified SP epitopes in the immune epitope database (IEDB) and immunogenicity in comparison with Mycobacterium tuberculosis (MTb) antigen matech epitopes in ten blood samples from both healthy individuals and tuberculosis patients. Moreover, invivo results in mice further validated the improved T and B- cell immunogenicity of different combinations of these VCs (Kovjezin et al 2013).

The aim of the present interaction with Aditec was to evaluate invivo the best dose and regimen for the induction of both cellular and humoral immune response by two sub-unit LP SP domains VCs against MTb. The VCs, named Mix #1 and Mix #2 contain respectively 4 or 2 MTb LP from known and novel NTb –derived antigens.

Assays conducted at Vaxil evaluated specific antibody production using an ELISA developed inhouse, while a team at the University of Sienna measured cytokine levels using Multiplex ELISA and ICS assays. Overall, humoral response was highly positive in selected dose and regimen of immunization comparing to that in control non-immunized mice.

Results on the cellular induced response by the VCs demonstrated a significant IL-2 production by CD4+ T cells vs. the control group. In addition, we observed an increase in IFN-gamma and IL- 12 production in individual mice compared to the levels in the control group. Lastly, we observed no difference in IL-4 and IL-6 production between immunized and control mice which is in line with previous results we published.

In summary, the Aditec grant is an important tool for investigation of basic keys in understanding the Immunological and potential clinical response to new therapeutics or preventive VCs.