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PPE18 protein of *Mycobacterium tuberculosis* inhibits CD4 T cell activation and B cell responses

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Scientists from DBT's research institute the Centre for DNA Fingerprinting & Diagnostics (CDFD), Uppal discovered that PPE18 protein (proline-proline-glutamic acid (PPE) family of proteins) inhibits both mycobacterial and non-mycobacterial (ovalbumin) antigen presentation by MHC class II molecules without affecting cell surface levels of MHC class II or co-stimulatory molecules. Team found that protein PPE18 does not affect presentation of pre-processed peptide or antigen uptake by macrophages but perturbs antigen degradation. Furthermore, the PPE18 protein inhibits acidification of phagolysosome, which could be the reason of inhibition of antigen degradation by PPE18. Since CD4 T cell influences B cell response which is important for anti-mycobacterial immunity.

Team also tested influence of PPE18 on B cell responses in mice, and the results indicated that PPE18 exhibited reduced maturation and activation of B cells and had decreased Mycobacteria specific IgM and IgG antibody titers. Thus, PPE18 is shown to reduce host adaptive immune responses. Our future studies are aimed at designing of novel therapeutics targeting PPE18.

The team has earlier shown that PPE18 protein of *Mycobacterium tuberculosis* activates the non-protective interleukin IL-10/T-helper (Th2-type) responses with simultaneous inhibition of the protective IL-12/Th1 responses. They showed that deletion of PPE18 from *M. tuberculosis* leads to decreased infection burden and reduced organ pathology in mice, resulting in the enhanced survival of the mice. These studies indicate that PPE18 probably plays an important role in mycobacterial virulence by manipulating host T cell and B cell adaptive immune responses. The class II antigen presentation and CD4 T cell response is known to be crucial to regulate anti-mycobacterial immunity. Thus, present was conducted investigate if PPE18 protein inhibits MHC class II-associated antigen presentation, CD4 T cell activation and subsequently the B cell responses.

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