SUMMARY

The development of an immune effector system depends on a complex network of interactions between different types of cells, which primarily include : T cells, B cells and macrophages and families of messenger molecules such as cytokines. Each type of immune cell specialises in a particular task : B cells produce antibodies, killer T cells destroy tumor cells or virus infected cells, helper T cells support and regulate the function of other immune competent cells. Macrophages not only eliminate bacterial, viral and protozoal infections by phagocytosis, but also present antigen to the T helper cells. Studies with murine helper T cell clones have shown that clones of TH1 subsets which secrete IL-2, IFN-γ, lymphotoxin, etc. are most effective in stimulating CMI response. In constrast, TH2 subset clones secrete IL-4, IL-5, IL-6 etc. are more efficient in promoting the secretion of antibodies. A number of recent studies, have focussed on the role of TH1 and TH2 cells, in resistence to infection. In certain diseases, the resolution of infection have been linked to the generation of TH1 cells and lymphokine, release typical to this subset. In malaria, both TH1 and TH2 cells seem to play an important role in generating protective immunity. Moreover, in case (toxins etc.) where antibody mediated immunity is required for their neutralisation, TH2 cells appear to play a significant role.

Since both these subsets of T helper cells recognise foreign antigens in association with class II MHC molecules bearing APCs such as macrophages and B cells, may play an important and distnic role in the activation of TH1 and TH2 type of helper T cells. Although both subsets respond and proliferate well to the antigens in presence of whole spleen cells as APCs, purified B cells and adherent cells induce optimal proliferation of TH2 and TH1 cells respectively.

The antigen-dependent T cells proliferation appears to require engagement of TCR complex by antigen associated with one of the major histocompatibility complex encoded molecule, and antigen-non-specific costimulatory signals provided by APC.

However, while the engagement of TCR with antigen is required for the initial steps in T cell activation, TCR crosslinking is not a sufficient signal to account for all the observed events that occur during activation. Moreover, TCR occupancy alone leads to T cell unresponsiveness. The nature of these costimulatory signals and their regulation is of considerable interest because they play a pivotal role in the generation and control of immune response.

The present study was aimed and designed to identify costimulatory molecules associated with cell surface membrane of LPS activated B cells. In order to achieve this, the molecules were isolated, reconstituted in PC vesicles and tested for their potential to generate costimulatory signal. Following facts have emerged from this study :

1. Three molecules, B1/B2/B3, falling in molecular weight range of 154, 104 and 35 kD respectively provide costimulatory signals to TH2 cells.
2. These proteins consist of single unit as demonstrated by two-dimensional SDS-PAGE in reducing conditions.
3. These molecules are present on B cells surface as treatment of B cells with pronase results into loss of these proteins.
4. These molecules bind to activated T cells more as compared to resting T cells, suggesting that ligands of these molecules on T cells are regulated and the extent of their expression depends upon the state of T cell.

5. Crosslinking of B1/B2/B3 to their ligand on TH2 cells in presence of first signal leads to T cells proliferation and secretion of IL-4, IL-5.

6. Signal generated by these proteins do not bring about a rise intracellular Ca^{2+} concentration but do mobilise the PKC from cytosol to the membrane of TH2 cells. They also phosphorylate tyrosine residues on proteins of higher molecular weight.

7. These molecules appear to be new costimulatory molecules based on their molecular weight (as discussed earlier).