4. Genesis of the thesis

Toxic Shock Syndrome a disease responsible for high morbidity i.e. it produces high illness with low mortality rate and is caused by Staphylococcal Enterotoxin B (Crass et al., 1986, Schlievert et al., 1986). SEB first binds to MHC-II outside the peptide-binding groove and to TCR (Dellabona et al., 1990) and produces cascade of events in both the cells (Hammerling et al., 1988). MHC-II ligation by SEB induces cAMP production and induces PKC mediated TNF-α in B cells (Hellendall et al., 1997, St. Pierre et al., 1991). These findings lead to the genesis of the work, as cAMP is the function of Gα subunit of heterotrimeric G proteins. Superantigens activate high number of T cells and cAMP elevating agents help in the presentation of antigen to T cells (St. Pierre et al., 1991). SEB induces cAMP in macrophages via PAFR, a GPCR that has already been implicated in various inflammatory responses (Honda et al., 2002).

SEB induced TSS is mediated by T cell (Uchiyama et al., 1989) but the involvement of macrophages has not been studied thoroughly as SEB first binds to MHC-II and then to TCR. SEB induced activation of macrophages does play an important role in TSS induction. Inhibition of SEB induced macrophage function prevents the induction of TSS in BALB/c mice when challenged with SEB.

IL-2 was reported as one of the first cytokine to be released from T cells and is responsible for the proliferation of T cells (June et al., 1987). But its direct role in SEB induced TSS has not been worked out. IL-2 directly mediate SEB induced TSS in BALB/c mice.