Toxic Shock Syndrome (TSS) is characterized by high fever, diarrhea, myalgia, capillary leakage and failure of various organs leading to death of an organism. TSS is caused by SEB; a 28 KD protein secreted by coagulase +ve Staphylococcal aureus strains. SEB an enterotoxin when ingested produces its effects in intestine; hence the name. SEB first binds to MHC-II on APCs and is then presented to T cells causing outburst of T cell proliferation. Superantigens activate around 5-30% of T cell population, which is much higher than normal antigen presentation. Since SEB can also activate around 5 % of T cell population, therefore it is also classified as one of the superantigen in the pool of superantigens. SEB binding to MHC-II initiates the cascade of events in APCs including generation of secondary messenger cAMP, which indicates the involvement of G proteins. Therefore the role of G protein in SEB induced TNF-α in macrophages was investigated and its subsequent effect on SEB induced TSS. G proteins do affect the SEB induced TNF-α in macrophages which is further affected by other molecules like TACE (TNF-α converting enzyme), EGFR (Epidermal Growth Factor Receptor), p38MAP Kinase and NFκB. These molecules are in sequence as inhibition of first molecule inhibits all other downstream molecules and TNF-α expression, the read out of the study.

T cells are known to mediate SEB induced TSS; therefore the effects of these inhibitors on T cells were investigated. Inhibition of MHC-II signaling intermediates also affected the course of T cell function i.e. SEB induced T cell proliferation and IL-2 production was reduced when T cells were cocultured with inhibitor pretreated macrophages. Inhibitors of these molecules affected the course of TSS induction when injected in mice before SEB challenge. G protein inhibitor abrogated the SEB induced TSS in BALB/c mice, while TACE inhibitor prevented about 60% of mice against SEB induced TSS. Though inhibition of EGFR induced some resistance in mice against TSS but could not prevent the induction of TSS. Similarly p38MAP kinase inhibition also induced some resistance in mice.

Since IL-2 is important for T cell proliferation, role of IL-2 in SEB induced TSS was investigated. It was observed that IL-2KO mice were resistant to SEB induced TSS and neutralization of IL-2 in vivo in BALB/c wild type mice prevented the induced TSS.