In this piece of work we have tried to study and understand the mechanisms regulating activation, death and memory commitment of CD4 T cells.

**Conclusions:**

**A. Role of PDE inhibitor, PF on CD4 T cell memory responses:**

1) Transient PF treatment early during immunization generates longer-lasting memory T cells *in vivo.*

2) PF treatment increases the frequency of antigen specific T cells without having any effect on clonal burst size of the proliferating T cells.

3) PF prolongs the survival of T cells by inhibiting post activation death, rather than T cell activation *per se.*

**B. Role of inducible nitric oxide synthase (iNOS) in T cell death and immune memory:**

1) In mice lacking iNOS, higher frequencies of CD4 memory T cells persist in response to immunizations.

2) Clonal burst size of antigen specific T cells does not differ between WT and iNOS−/− mice.

3) In iNOS−/− mice, CD4 T cell memory is enhanced even if iNOS+/+ sufficient APCs are used for immunization, indicating that the effect is T cell autocrine.

4) iNOS−/− T cells show greater persistence of memory even in iNOS+/+ microenvironment, supporting that iNOS in T cell is determinant of CD4 T cell memory.

5) MnTBAP (peroxynitrites scavenger) protects CD4 T cells from post activation TSWD (death by neglect) in mouse as well as human T cells.
6) Enhanced persistence of CD4 T cells is due to difference in cell survival and not due to the difference in primary T cell activation and proliferation.

**C. Effect of aging on T cell responses:**

1) Aged C57BL/6 mice show less frequencies of peripheral CD4 and CD8 T cells and B cells, but higher frequency of macrophages in the spleen as compared to that from young C57BL/6 mice.

2) T cells from aged mice show delay in activation marker upregulation and proliferation as compared to T cells from young mice and this delay is partially rescued with exogenously fed IL-2.

3) T cell death whether AICD or TSWD is comparable between aged and young mice.

4) There is higher frequency of CD44hi T cells in aged mice as compared to young mice.

5) T cells from aged mice show lower T_cM:T_EM ratio as compared to those from young mice.

6) Aged mice show poor memory response in terms of T cell proliferation and IFN-γ secretion in response to *in vivo* immunization.

**D. Effect of IL-2 absence on T cell responses:**

1) c Rel^+/− mice (deficient in IL-2 synthesis) show less frequencies of peripheral CD4 and CD8 T cells as compared to that from WT C57BL/6 mice.

2) T cells from c Rel^+/− mice show delay in activation marker upregulation and proliferation as compared to those from WT mice and this delay is partially rescued with exogenously fed IL-2.

3) T cell death whether AICD or TSWD is comparable between WT and c-Rel^+/− mice.

4) T cells from c-Rel^+/− mice show marginally low T_cM:T_EM ratio as compared to those from
WT mice.

**E. T cells as antigen presenting cells:**

1) IA$^b$ expressing naïve and activated T cells from JLA mice could prime responder T cells as well as professional APCs, rather than inducing anergy in responder T cells. This is true for presentation of both alloantigens and conventional protein antigens to responding T cells.