Abstract: A unique feature of T-cell development is the central role played by clonally distributed T-cell receptors (TCR), which are encoded by somatically rearranged gene segments that produce a diverse, non-germline encoded set of receptors. Fate determination in individual T-cells is mediated by ligand-receptor signals that arise from unprogrammed genetic interactions, under conditions in which the relevant ligand concentration and the receptor affinity are not evolutionarily controlled. A precursor T-cell with a TCR that either fails to demonstrate appreciable self-reactivity or binds with high affinity to reasonably abundant self-peptide major histocompatibility complex (MHC)-ligands will undergo apoptosis. In contrast, a precursor T-cell that shows lower affinity to moderately abundant ligands will receive suitable signals for survival and maturation. Recently, we have developed a rapid in vitro two-step organ culture system that permits homogeneous populations of non-transformed precursor T-cells to undergo selective commitment to the CD4 or CD8 lineage. Using this model, we have shown that the choice of positively selected ab T-cells between the CD4 helper and CD8 cytotoxic lineages is regulated by the TCR signaling duration in response to self-peptides bound to the MHC. J. Med. Invest. 49: 1-6, 2002

Keywords: thymocytes, lineage commitment, T-cell receptor
The Journal of Medical Investigation Vol. 49 2002

2-stage thymocyte culture system

1st stage

- DP cells are committed into CD4 or CD8 T-cell lineage dependent on duration of TCR signaling even if coreceptor (CD4 or CD8) is not silenced

2nd stage

- The coreceptor (CD4 or CD8) is silenced and lineage specific functions are acquired dependent on TCR signaling

Aquisition of MHC specificity by TCR recombination

- CD4+CD8+ cells
- TCR rearrangement
- Class II binding 
  - survival / CD8 silencing
  - CD8+ cells
  - no class II binding 
  - death
- CD4+CD8+ cells committed to CD8 lineage
- TCR
- short TCR signal
- long TCR signal
- CD4
- CD8
- no class I binding 
  - death
- CD4+CD8+ cells committed to CD4 lineage
- TCR
- CD4
- CD8
- class I binding 
  - survival / CD8 silencing
  - CD4+ cells
- no class I binding 
  - death
- CD8+ cells