Th1, Th2 and Th17 polarized T cell lines have distinct cytokine profiles. Th1 and Th2 cells have different expression of co-stimulatory molecules (Th1 > Th2 for OX40, ICAM-1, CD5, and CD40L; Th2 > Th1 for ICOS) which supports the hypothesis that they interact at differing avidities.

Table 1. CD4 T cell lines selected against the same pMHC under Th1(A), Th2(B) and Th17(C) polarizing conditions evolve the expansion of highly distinct, dominant TCR usage. CDR3 length for Th2 > Th1 > Th17.

TCRα sequencing shows distinct CDR3α selection from the available repertoire. Th2 tend to be elongated Th2 derived TCRα transgenic with elongated CDR3α region made (construct strategy – Figure 2).

Figures 7 and 8. TCR transgenic with elongated CDR3α and β partner chains – TCRαβ primed with IFA make enhanced T cell responses to peptide and Th2 cytokines (IL-4, 5, 9, 10, 13), but no IFNγ or IL-17.

A relationship between TCRαβ choice, cytokine polarization and avidity?

Figures 3, 4 and 5. Restimulation in vitro shows progressive focusing of favored TCRβ partner chain with the adoption of a Th2 cell phenotype (IL-4, 5, 9, 10, 13 and no IFNγ) and up-regulation of GATA-3 transcription progressively up-regulated.

Figures 6 and 9. TCR transgenic with elongated CDR3α region made (construct strategy – Figure 2).

Th2 derived TCRαβ has low avidity. Tetramer binding studies of cells from Th1/Th2/Th17 polarized T cell lines and TCRαβ transgenic non-transgenic controls, while either Th2 polarized lines or cells from Th2 derived TCRαβ transgenics responded by making cytokine, binding studies indicate an avidity spectrum Th17 > Th1 > Th2. No evidence of cytokine storm or thymocyte depletion.

From Boyton et al. 2002. Lack of support for an alternative model whereby Th2 polarization is a stochastic outcome of thymocyte depletion following a peptide-induced cytokine storm.