IEL / LPL
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T.69. The Role of the Two Isoforms of Pre-T Cell-receptor-alpha in Unconventional T Cell Development

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TCRγδ+ cells and TCRαβ+CD8αα+ intraepithelial lymphocytes (IELs) of the gut are unconventional T cells that reside in tissues and provide innate-like immune responses to "stressed-self." As these cells share common functional properties in the periphery, we have hypothesised a common mechanism of development in the thymus; their progenitors diverging from the conventional T cell developmental pathway based on TCR signal strength at the DN stage. The pre-T-alpha chain (pTα) that pairs with TCRβ to generate the pre-TCR, has two isoforms; pTαa and pTαb. Both can form a functional pre-TCR with TCRβ, but these are expressed at the cell surface at different levels and are thought to have different signalling capabilities. We hypothesise that pTαa and pTαb permit differential signal strength through the pre-TCR at the DN stage, facilitating the divergence of the conventional and unconventional lineages of TCRαβ+ T cells. Preliminary data in fetal thymic organ culture suggest that pTαa and pTαb are differentially expressed in WT thymocytes, and may differentially regulate T cell development. In addition, BAC transgenic mice that express singly either pTαa or pTαb under the pTα promoter are being generated to fully characterise their role in conventional vs. unconventional lineage commitment. Here, we report our preliminary findings.

T.70. Importance of IEL Response During *Encephalitozoon Cuniculi* Infection is CCR7 Dependent

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Per-oral *Encephalitozoon cuniculi* infection induces a strong IEL (intraepithelial lymphocyte) response in the gut. Although importance of IEL in protective immunity against other gut pathogens has been reported, mechanism responsible for the priming of these cells or antigen-presenting cells involved in the process remains enigmatic. Role of inflammatory chemokines in the recruitment and localization of dendritic cell as well as naïve T cells to the sites of inflammation and infection is well documented. Of particular interest, recent studies have demonstrated the importance of CCR7 in gut mucosa trafficking. Upon gut infection, Peyer's patch dendritic cells from CCR7-/- mice are unable to be recruited to mesenteric lymph nodes (MLN) and naïve T cells repopulation of MLN is also defective. Down-regulation of both MLN and IEL response to *E. cuniculi* infection was observed in CCR7-/- mice. As compared to wild type littermates lower influx of all IEL subsets was observed in CCR7 deficient mice and mutant animals exhibited lower IFNγ production in mucosal (MLN and IEL) compartments. These data suggests that CCR7 is involved in the priming and/or recruitment process of IEL to the gut after *E. cuniculi* infection.

T.71. CD8+ CD101+ Regulatory T Cells in the Intestine: Generation and Characterization of Cell Lines and the Identification of Defects in IBD

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Freshly isolated CD8+ LP T cells (that have been in contact with IEC) from normal individuals have been shown to have a regulatory function. To study the mechanism by which the CD8+ T cells mediate suppression, we established conditions required to generate cell lines. Freshly isolated LPL cells were stimulated with a humanized anti CD3 Ab, for 5 days followed by addition of IL7, IL15 and irradiated PBMCs. 10 days later CD8+ T cells were purified and generated a cell line in the presence of IL7 and IL15. Lines were assessed for ability to inhibit CD4+ T cell proliferation. Lines from normal and UC patients were able to suppress, in a contact dependent fashion. Interestingly, lines generated from CD patients showed lower capacity to suppress. Lines from all 3 groups express CD3, CD8β, CD2 and CD101. We screened mABs against CD8+ cell line for their ability to block suppression. Serum from mice immunized with CD8+ lines that suppressed (but not pre-immune sera) was able to reverse suppression by the lines. CD8+ regulatory T cells may be an important population involved in maintaining mucosal homeostasis since only CD8+ T cell lines from CD patients fail to mediate suppression.