

**V α 24⁺ T-cells are deficient and have defective
interleukin-4 and interferon- γ production in
inflammatory bowel disease**

RH Grose, FM Thompson and AG
Cummins

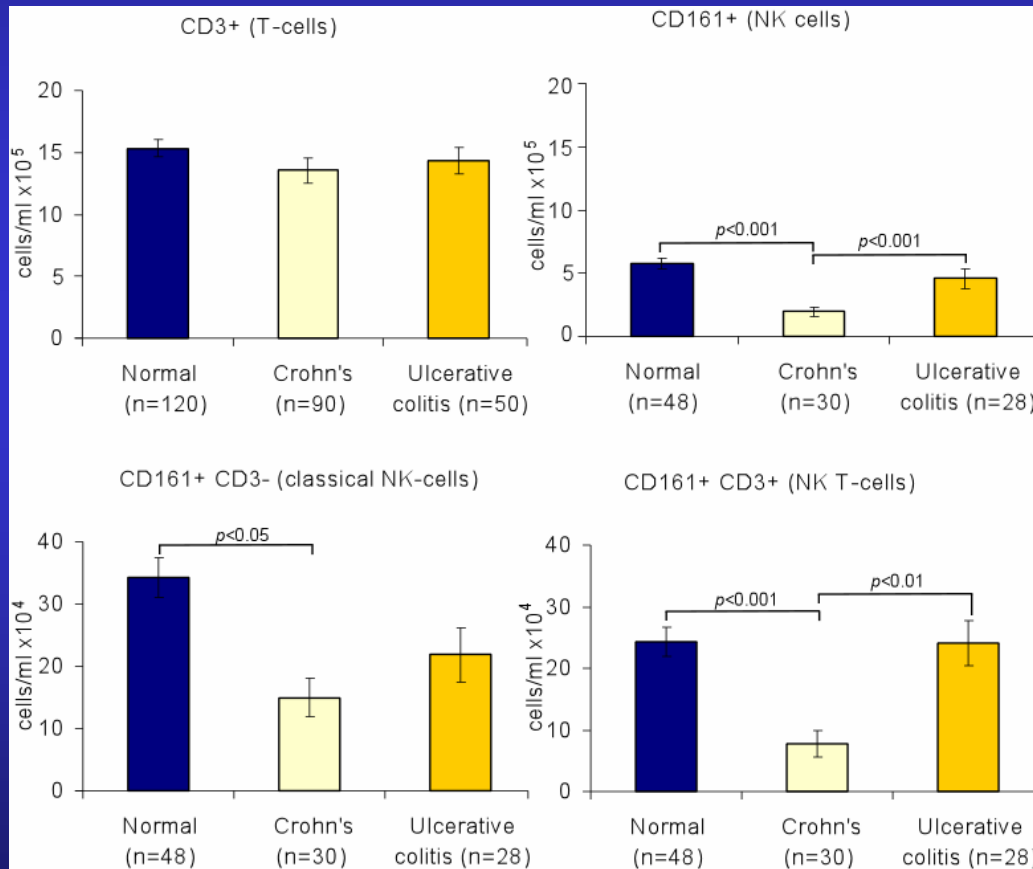
What are NK T-cells?

- Surface phenotype of NK (CD161) and T-cells (CD3)
- Uniquely have an invariant $V\alpha 24J\alpha Q$ chain that pairs with the $V\beta 11$ chain of the CD3 receptor
- Recognise glycolipid antigens mimicked by the marine-derived α -galactosylceramide
- CD1d restricted (dendritic cells)
- Therefore defined by CD1d/ α -galactosylceramide tetramers

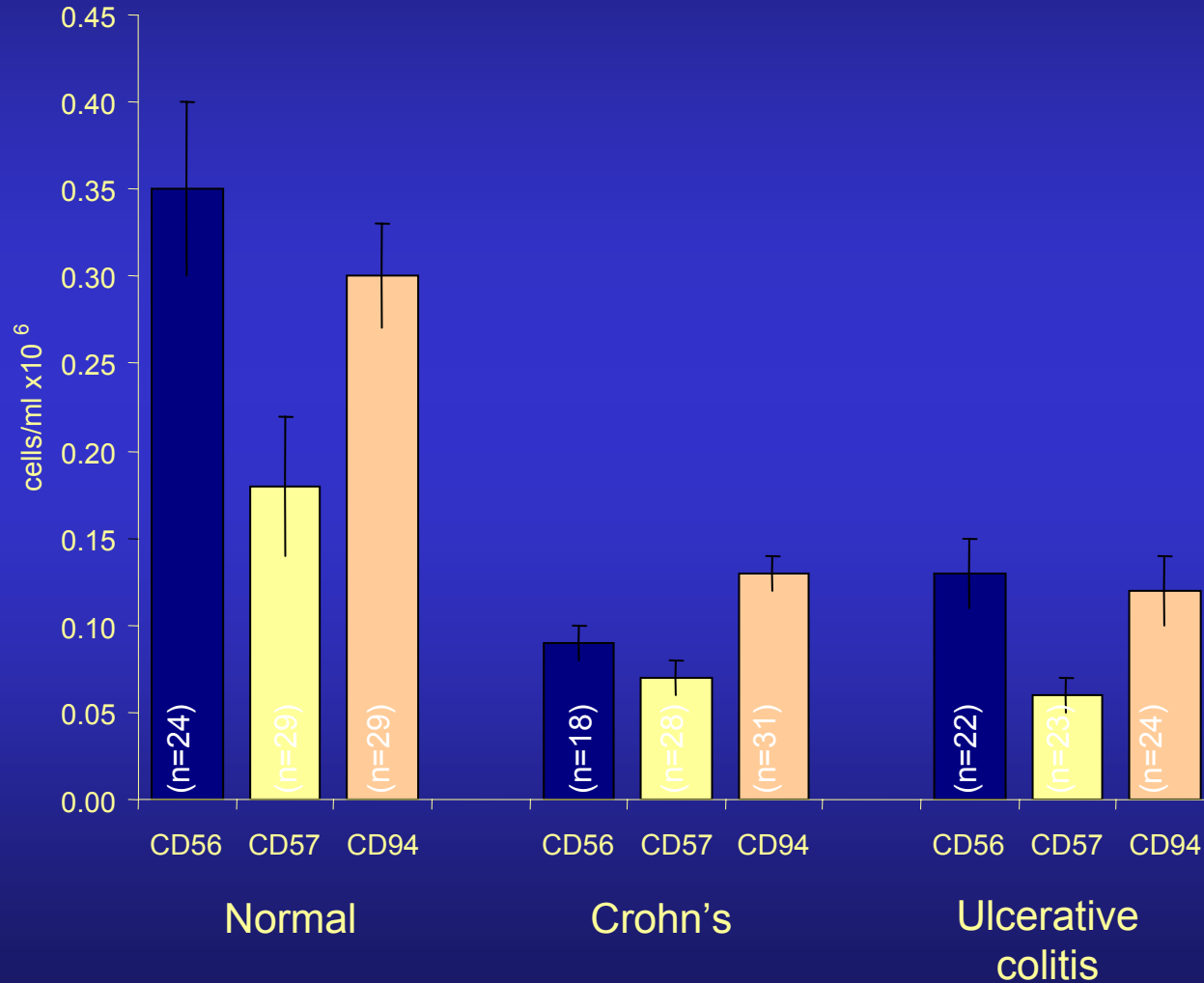
How does this relate to immunoregulation?

- Hypothesis is that NK T-cells recognise membrane glycolipids exposed during tissue damage (eg viral infection)
- Down-regulate excessive and inappropriate immune activity

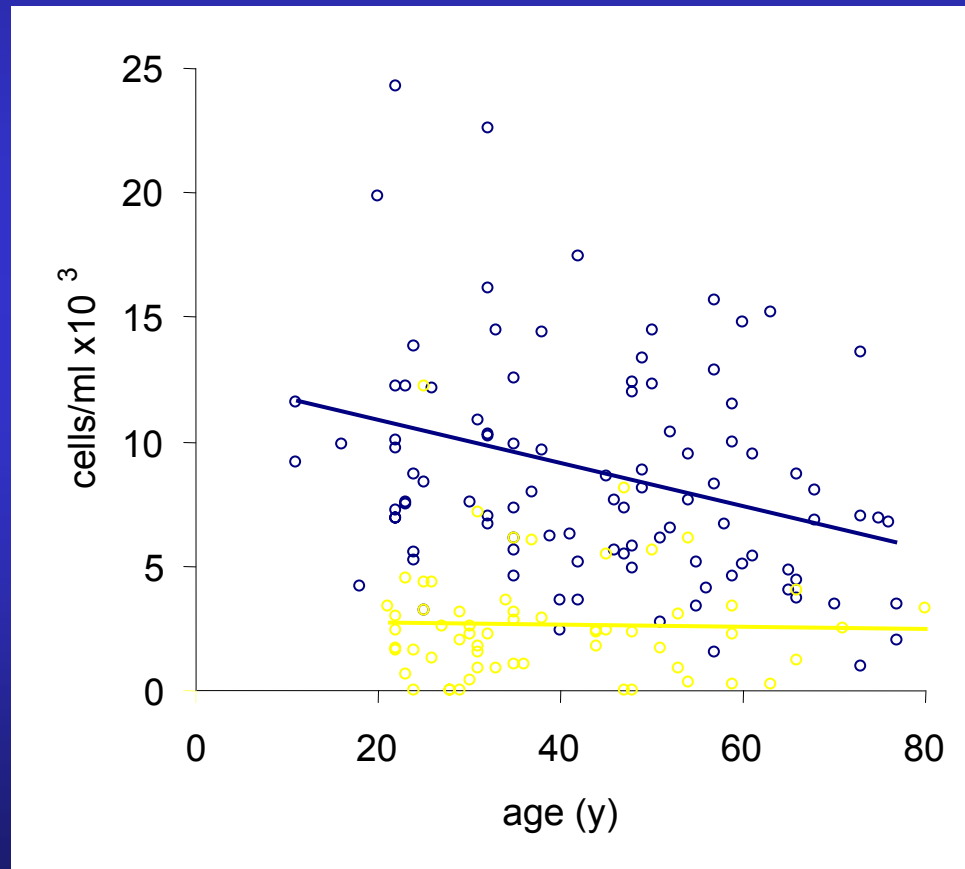
Comparison of T-cells, NK cells and NK T-cells in inflammatory bowel disease



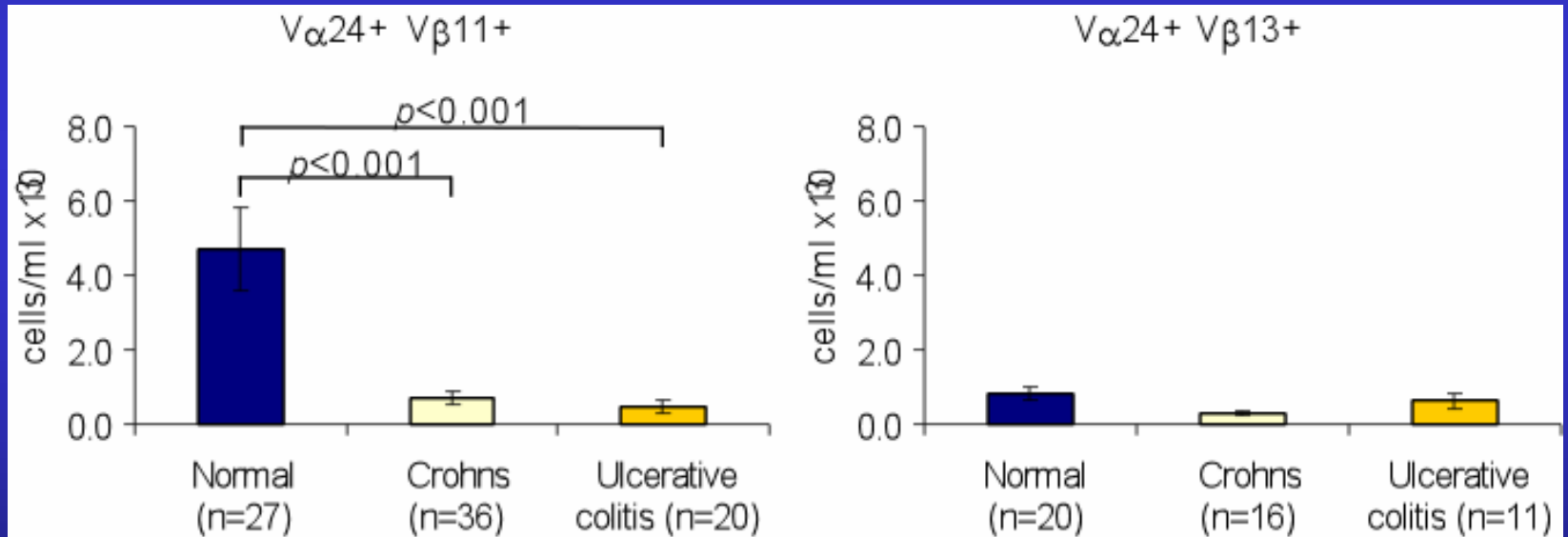
Comparison of NK cells in inflammatory bowel disease



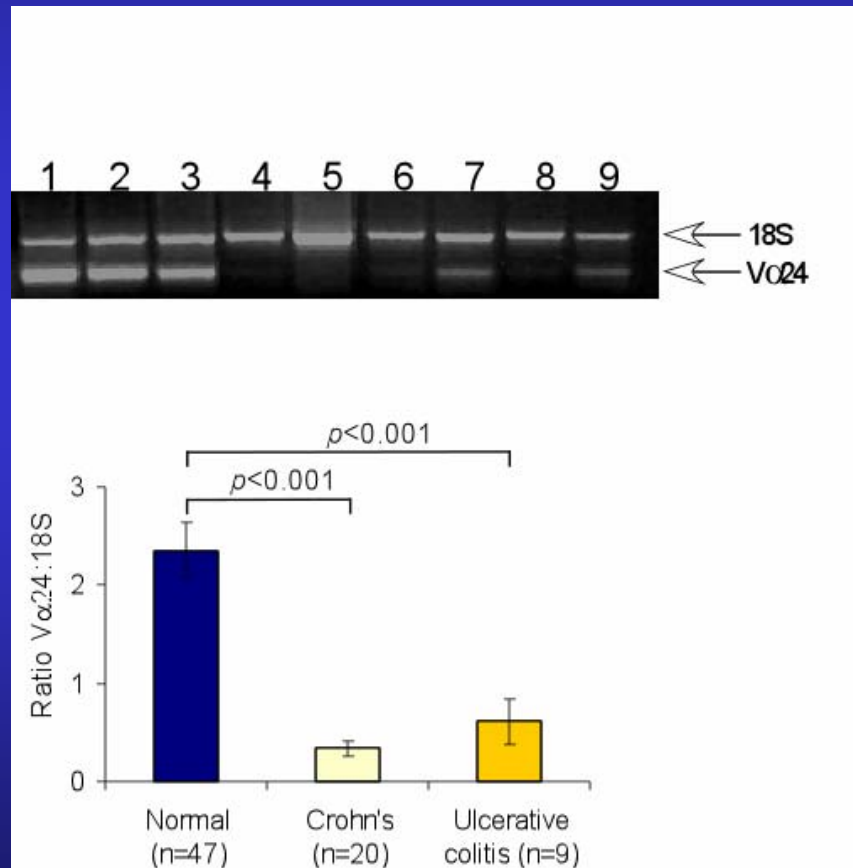
Comparison of $V\alpha 24+$ T-cells in control subjects and in Crohn's disease



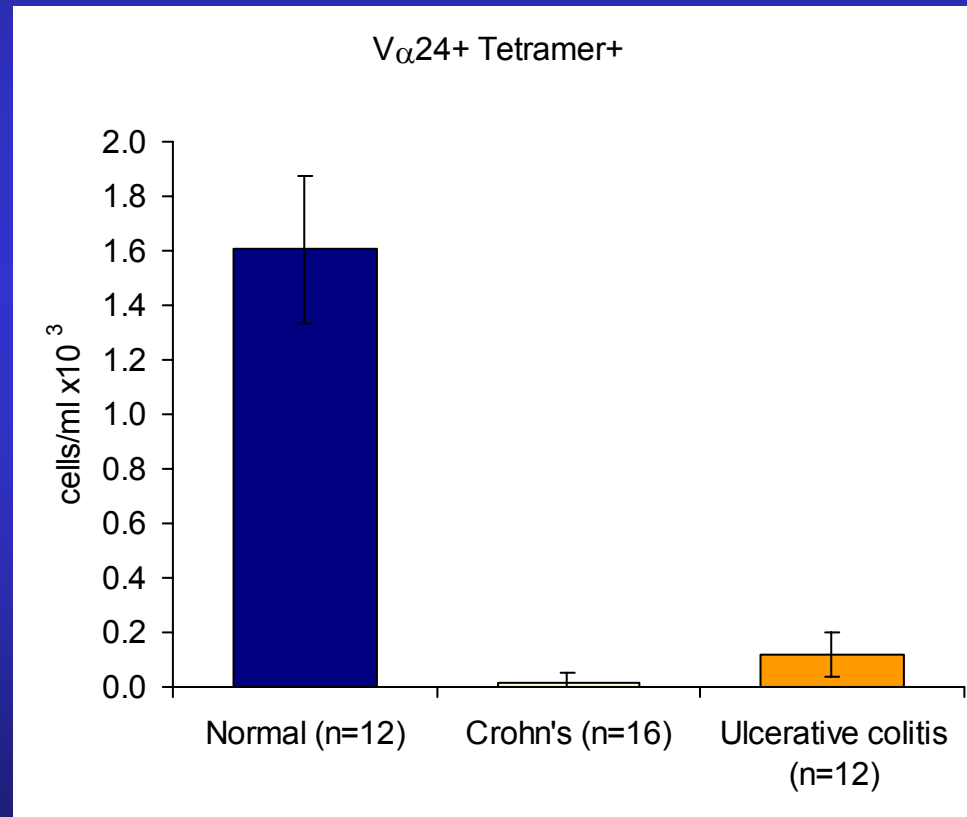
Immunoregulatory V α 24+ T-cells Subsets



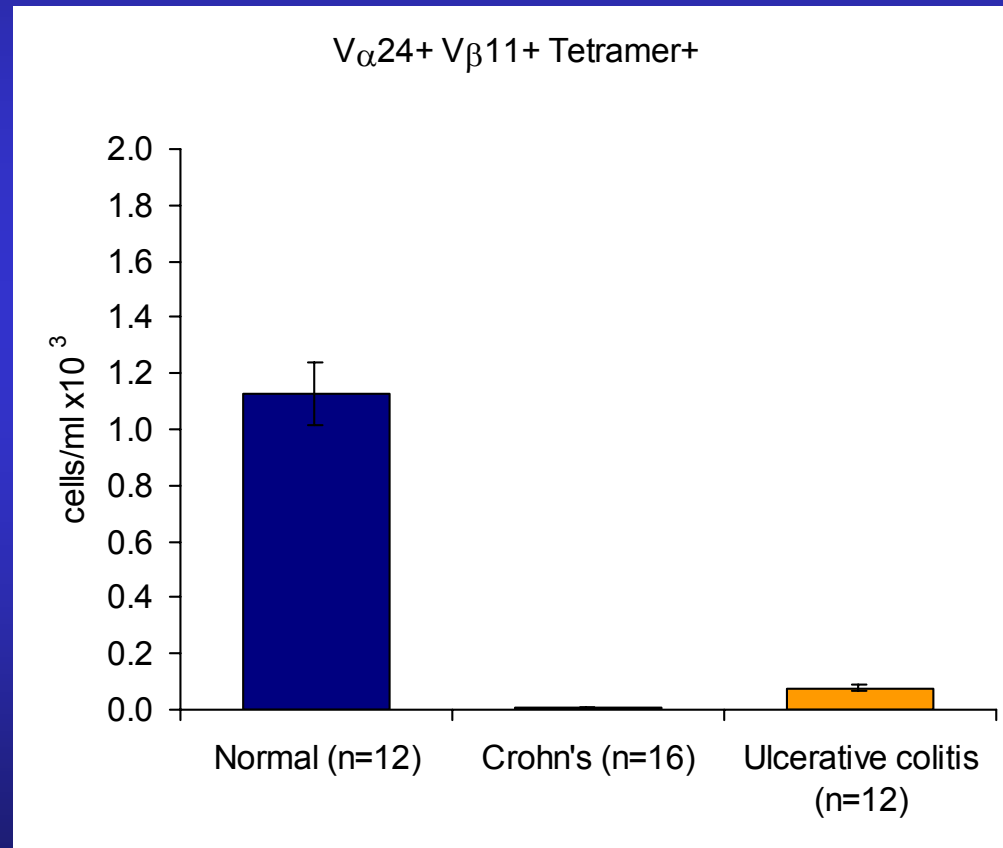
mRNA expression of V α 24 in Ileocolonic Biopsies



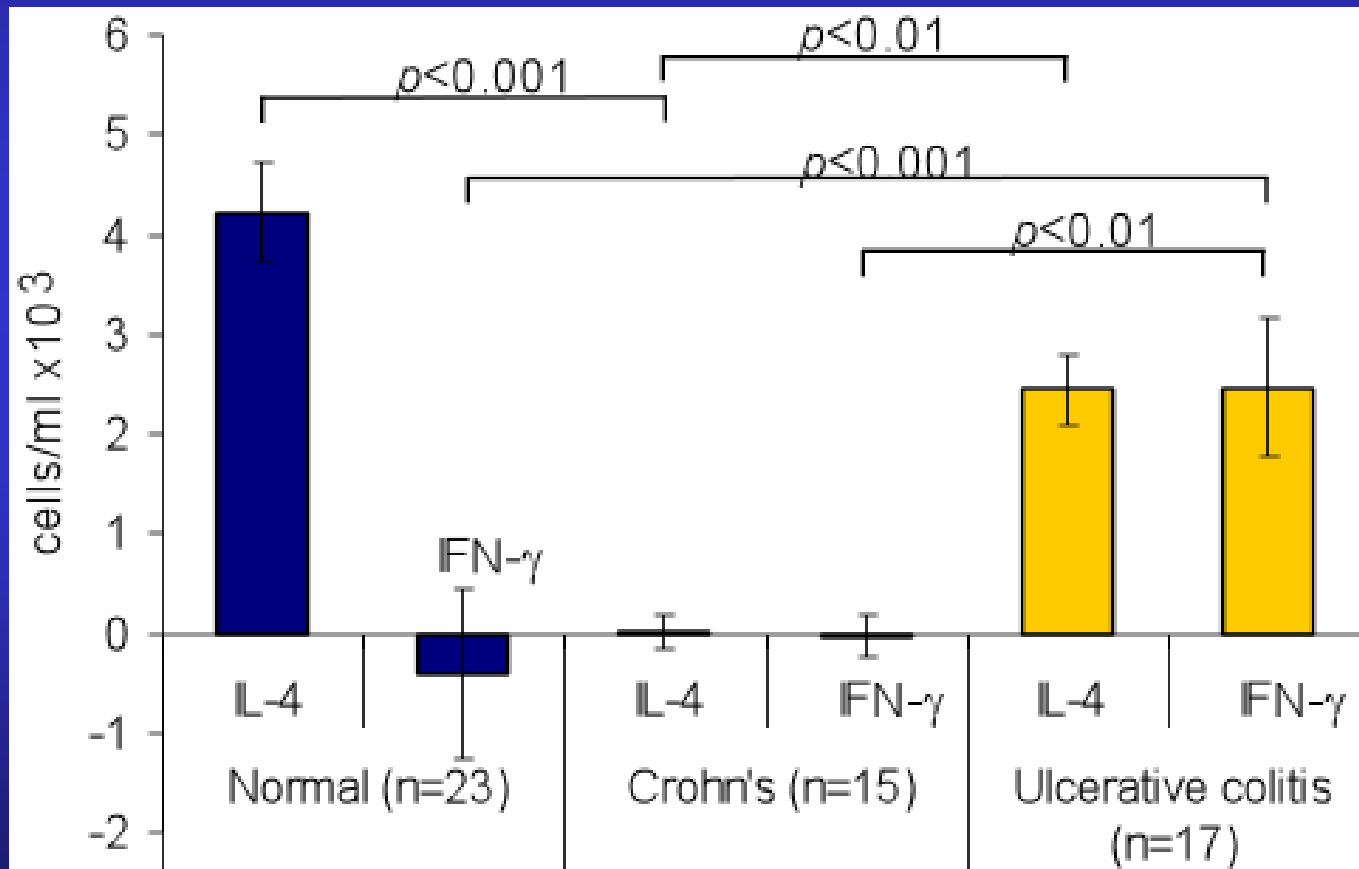
Comparison of α -GalCer/CD1d tetramer positive $V\alpha 24^+$ T-cells



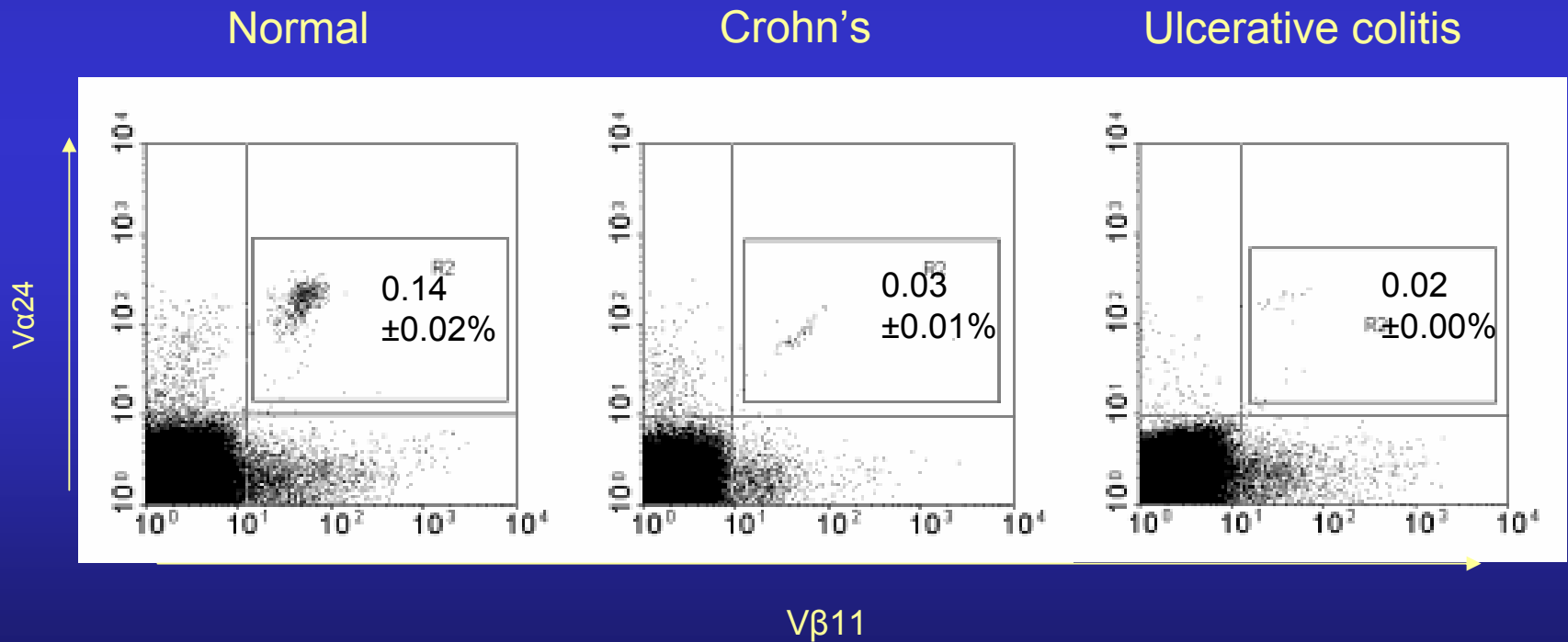
Comparison of α -GalCer/CD1d tetramer positive $V\alpha 24+$ $V\beta 11+$ T-cells



Comparison of intracellular cytokine production in $V\alpha 24^+$ T-cells



Comparison of IL-4 intracellular staining in V α 24+ V β 11+ tetramer+ T-cells



Conclusions

- CD56, CD57, CD94, CD161 NK cell deficiency in Crohn's disease
- CD161+ CD3+ T-cell deficiency in Crohn's disease
- V α 24+ T-cell deficiency in Crohn's disease systemically and mucosally
- V α 24+ V β 11+ tetramer+ T-cell deficiency in both Crohn's disease and ulcerative colitis
- Functional IL-4 cytokine deficiency in V α 24+ V β 11+ tetramer+ T-cells in both Crohn's disease and in ulcerative colitis