

IL-17 Secreting CD8 T Cells (Tc17)

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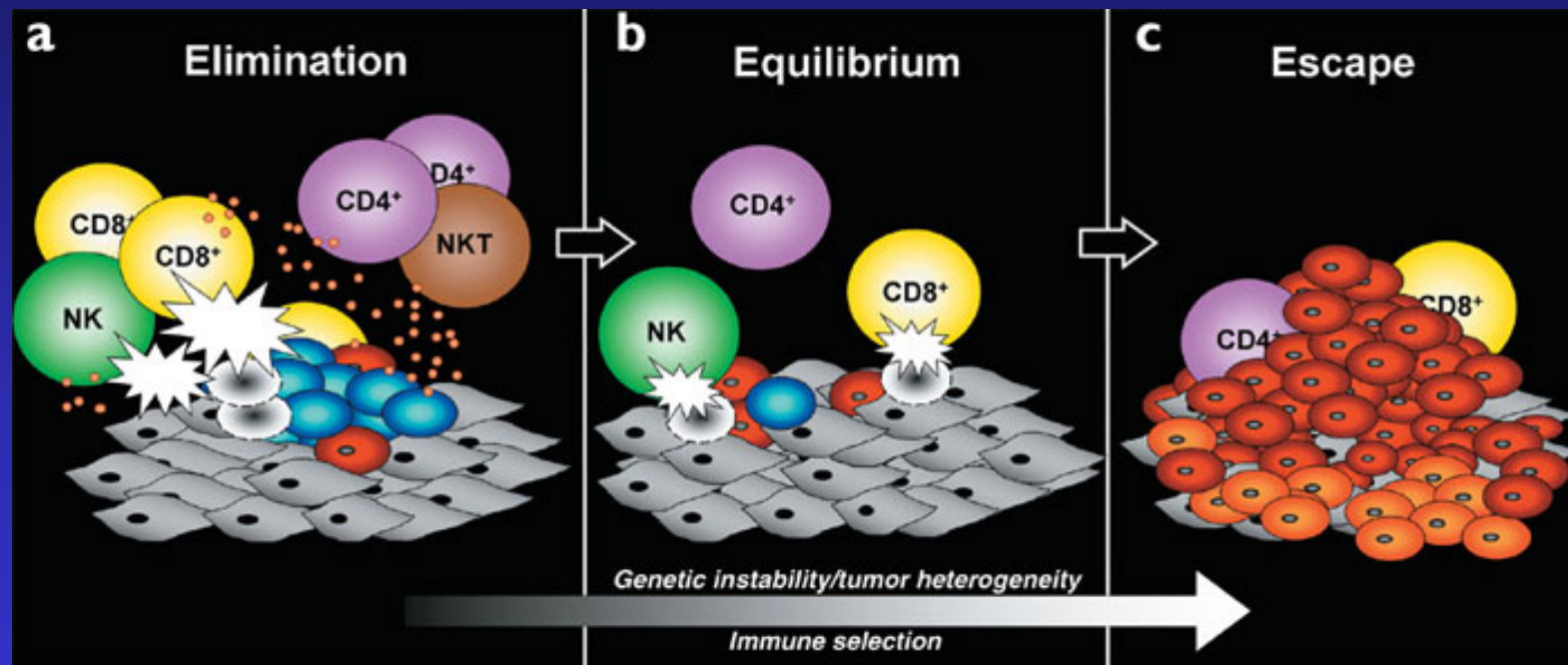
Disclosure Of Financial Relationships

- Consulting:
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- Sponsored Research Agreements:
Medarex Inc
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- Patents
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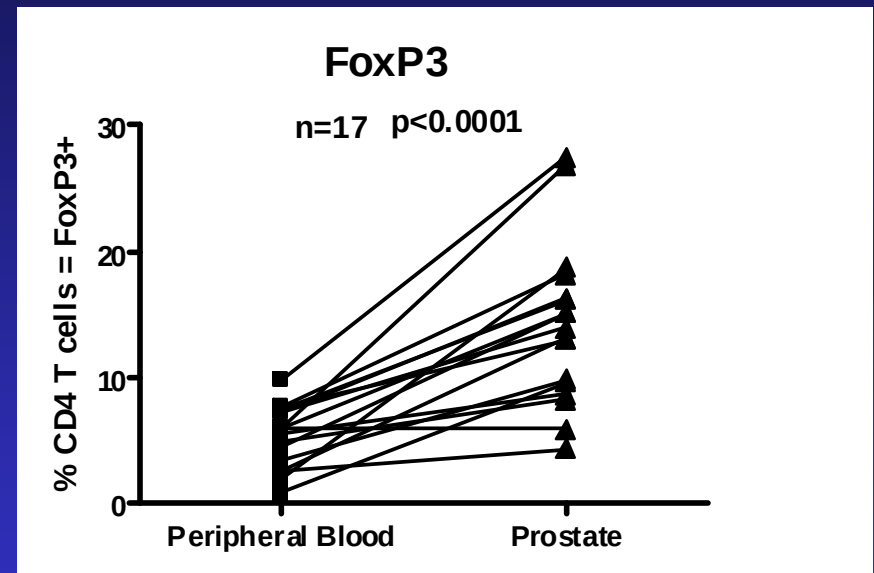
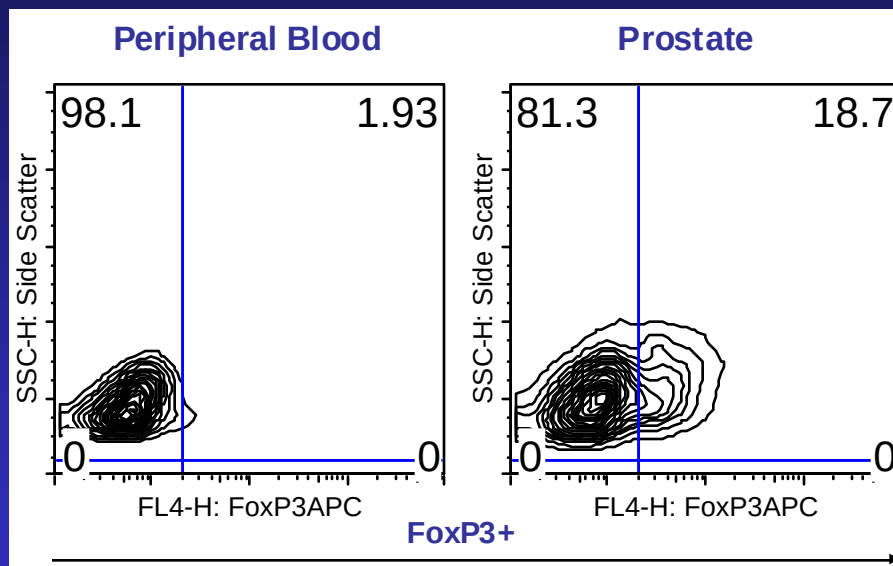
Objectives

- A. Briefly describe the CD4 T cells that infiltrate the prostate gland in men with cancer
- B. Introduce the concept of CD8 T cells that secrete IL-17
 - 1. Conditions for Induction
 - 2. In vitro- transcriptional profile
- C. In vivo function of Tc17
 - A. Self-antigen
 - B. Tumors

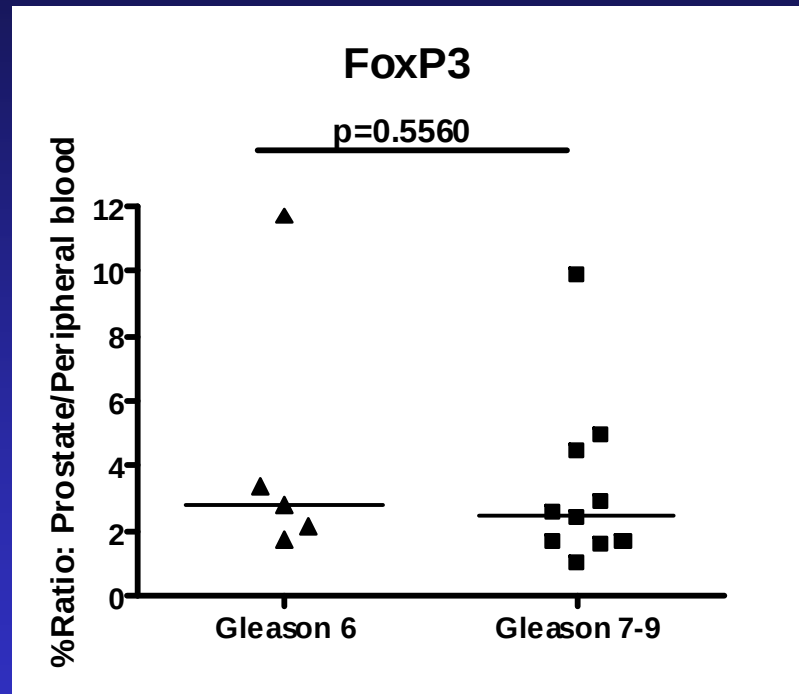
Tumor Surveillance



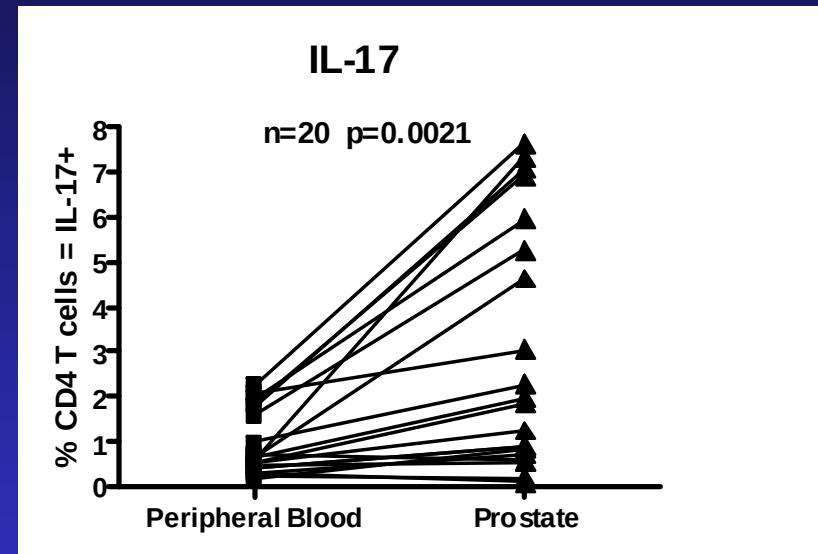
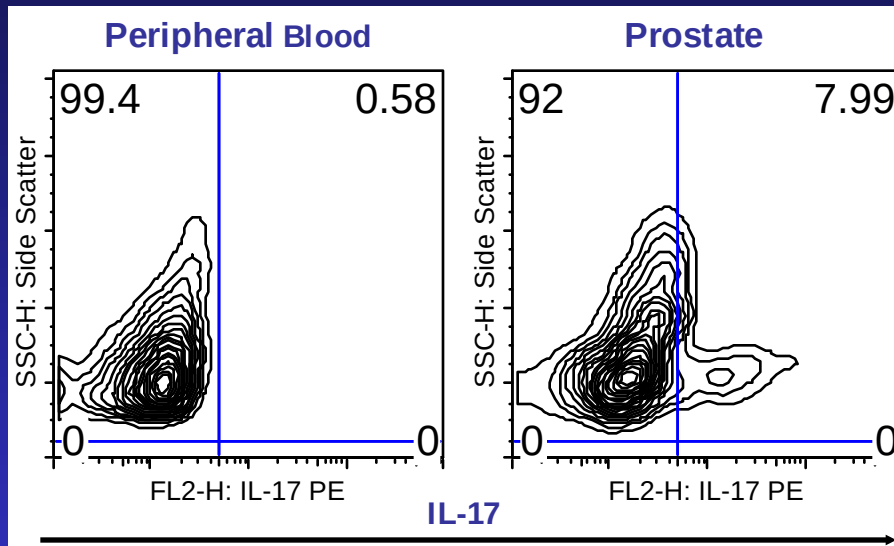
Prostate Cancer: Treg Infiltration



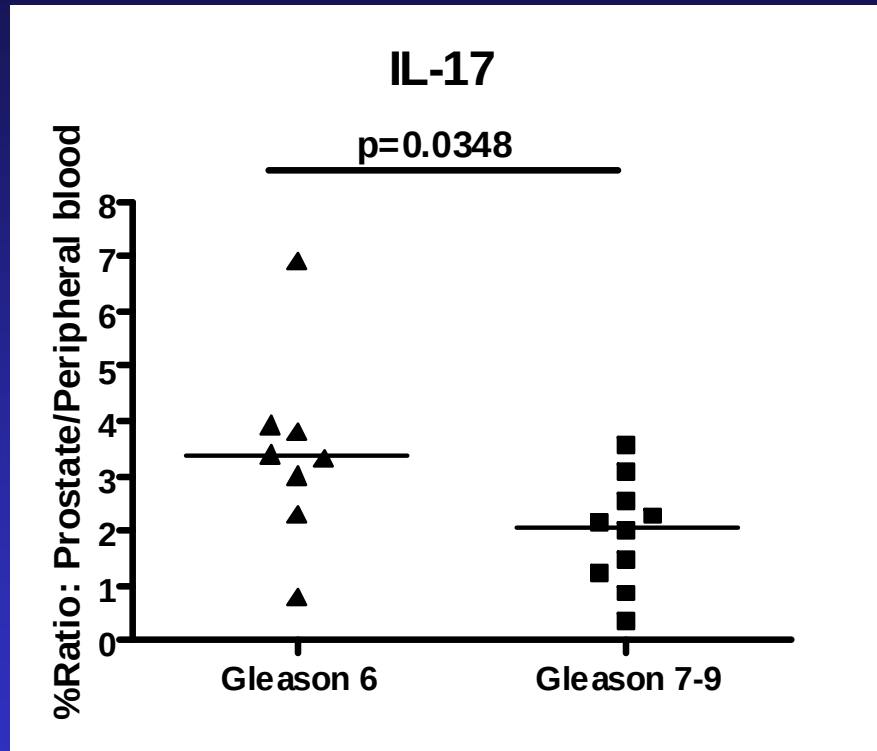
Treg: Correlation with Gleason Grade ?



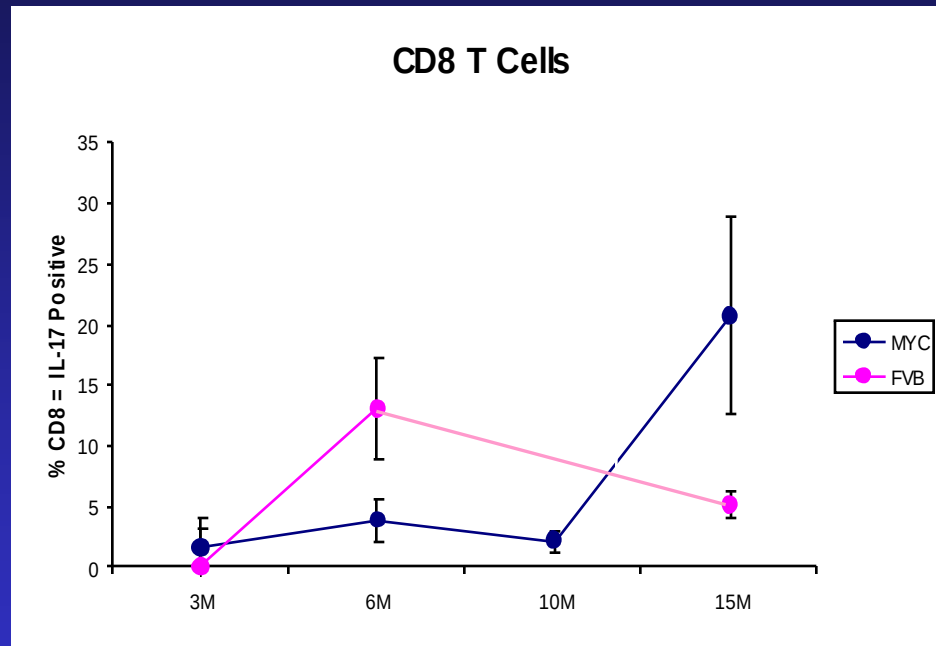
Prostate Cancer: TH17 Infiltration



T_{H17} : Correlation with Gleason Grade ?

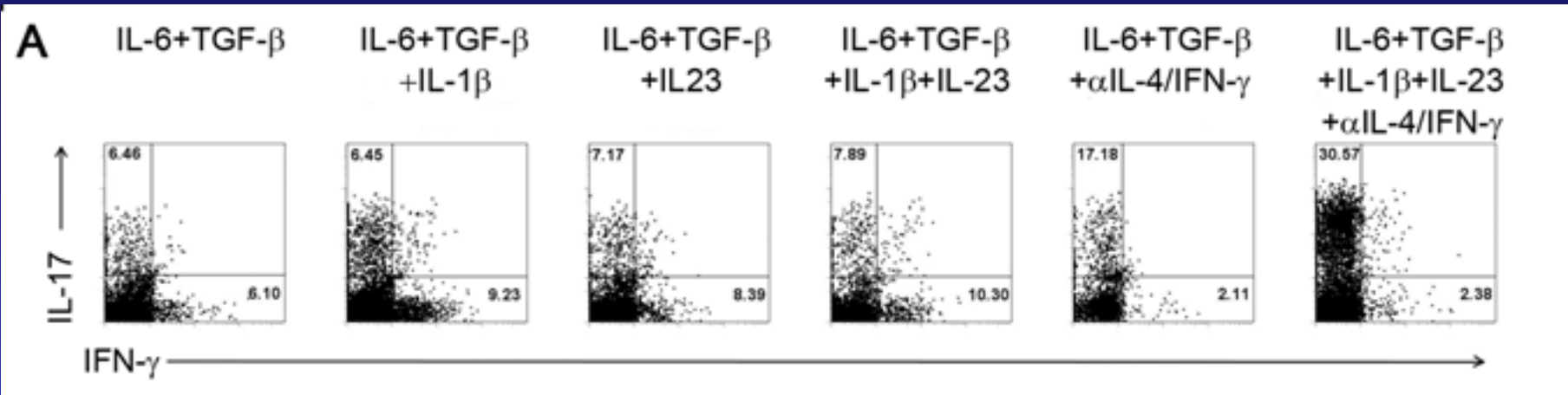


Tumor-Infiltrating, IL-17 Producing CD8 T Cells (in mice)

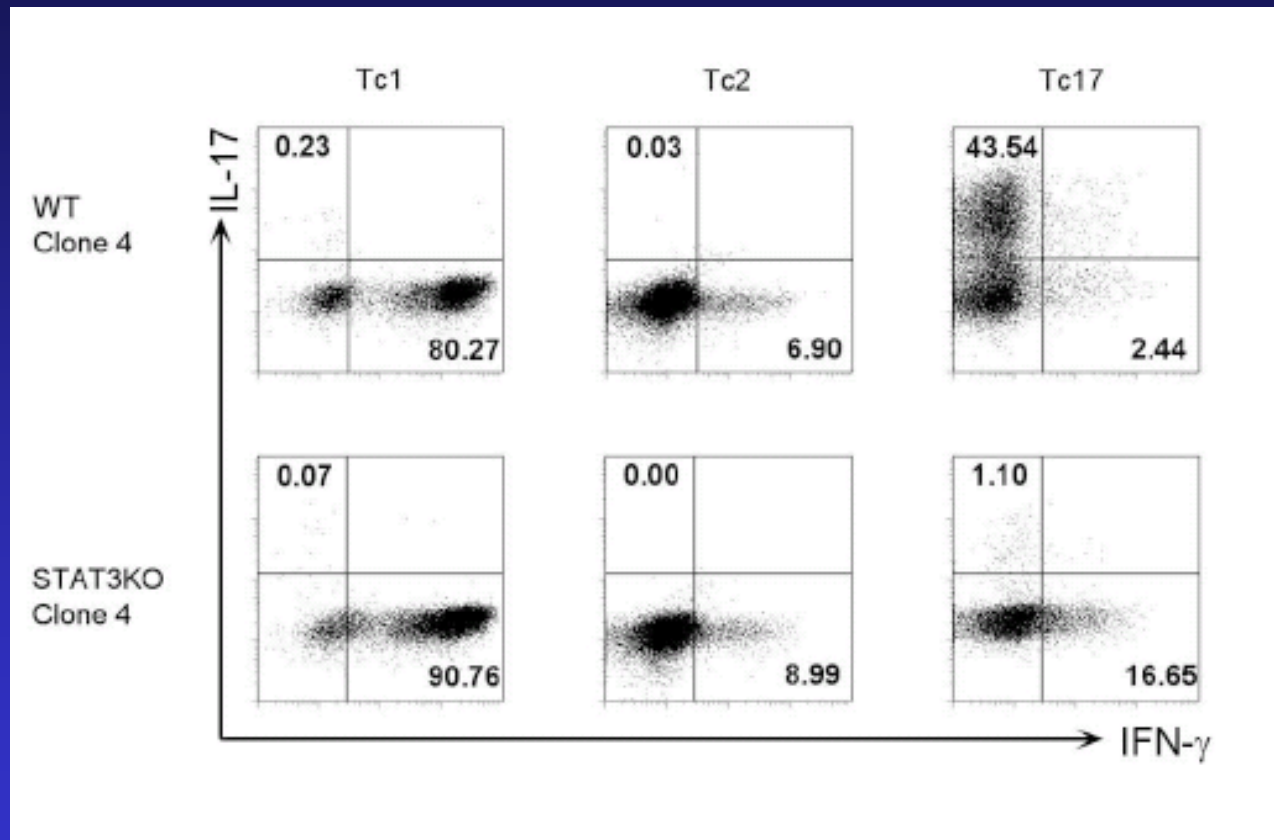


MYC = Probasin – MYC (Tumor Bearing)
FVB = Nontransgene-bearing littermate

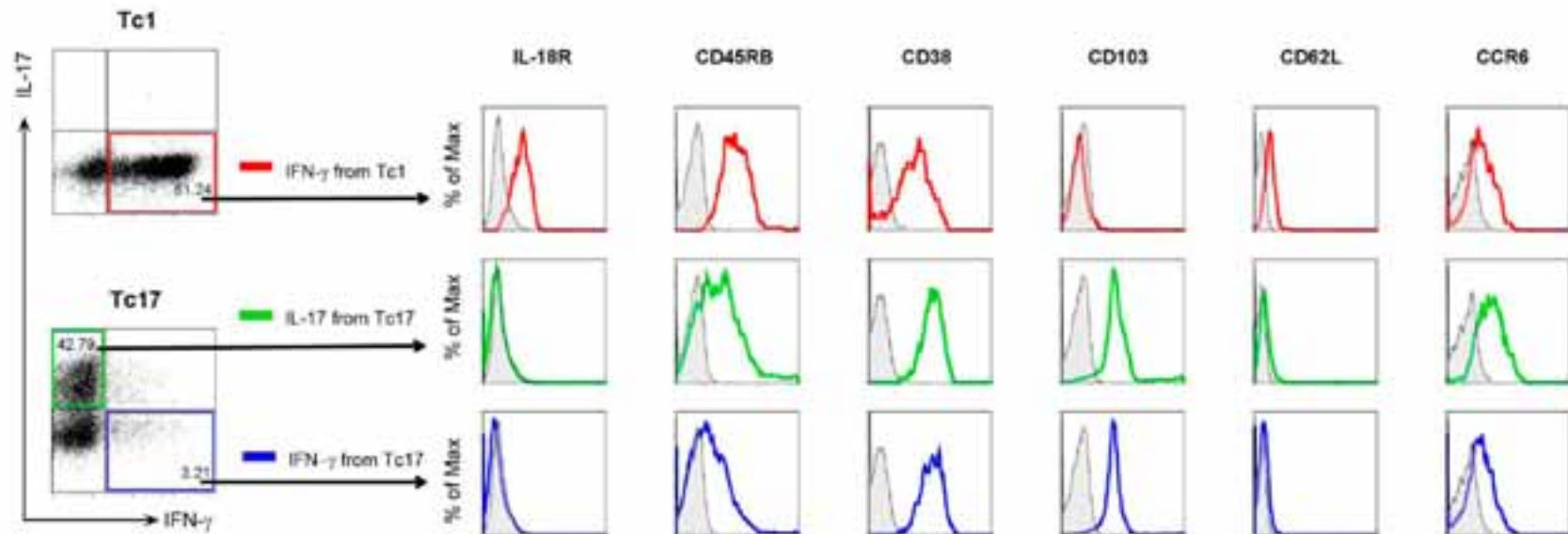
Can CD8 Be Induced to Secrete IL-17 ??



STAT3 is Required for Tc17 Differentiation

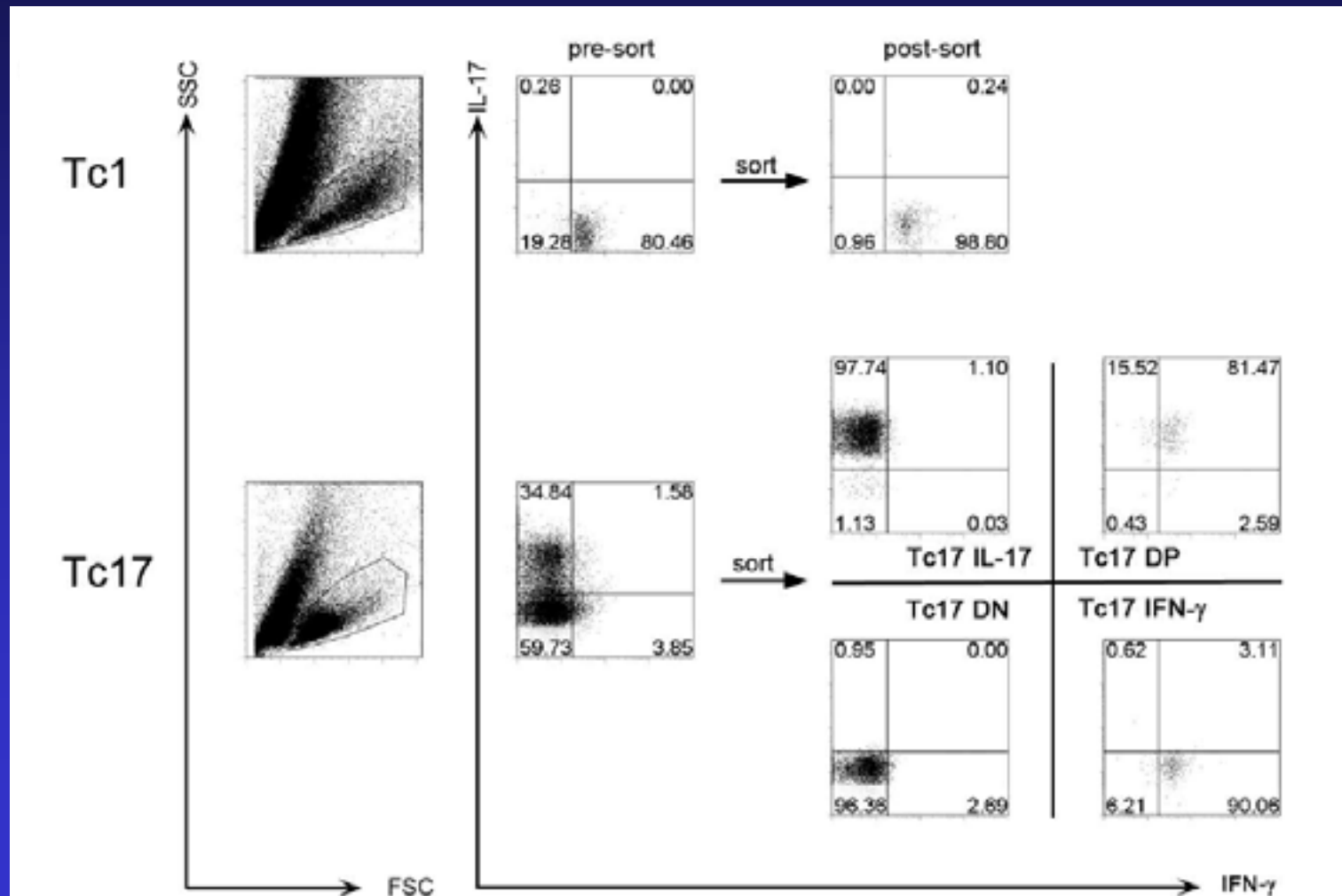


Sorting Out Tc17 ?

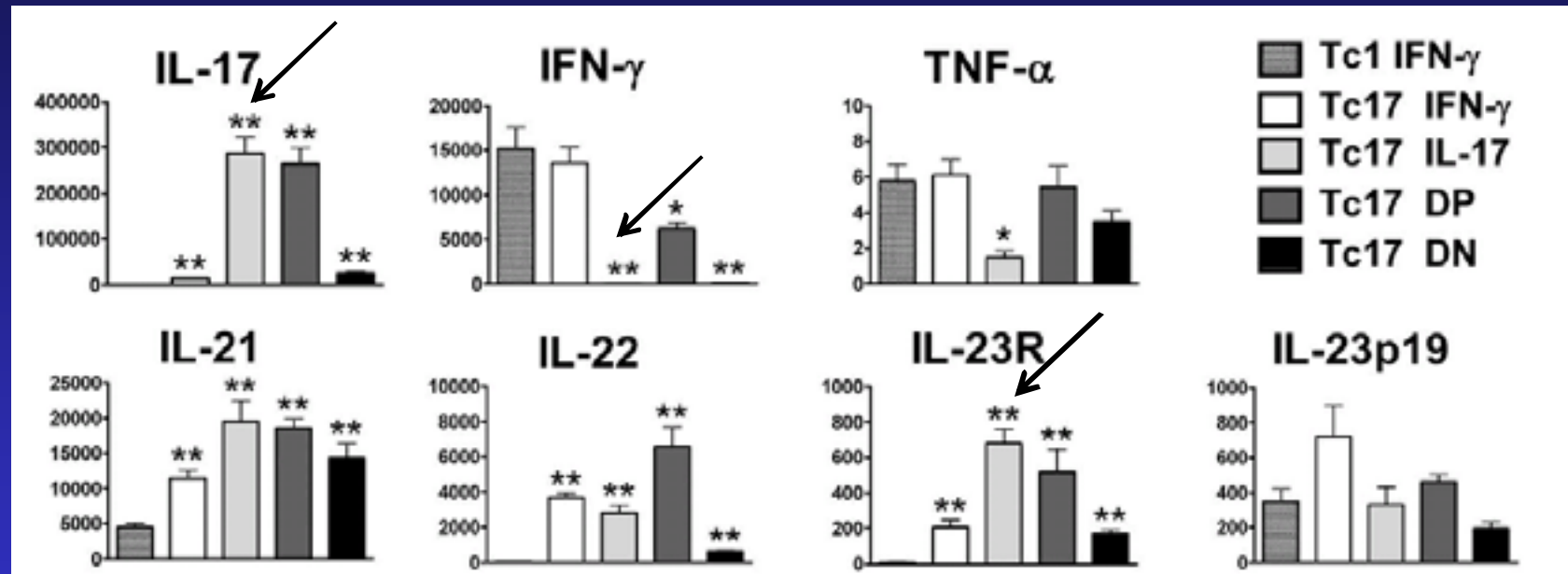


Bottom Line – No way to separate Tc17 conditioned gamma secretors from IL-17 secretors !

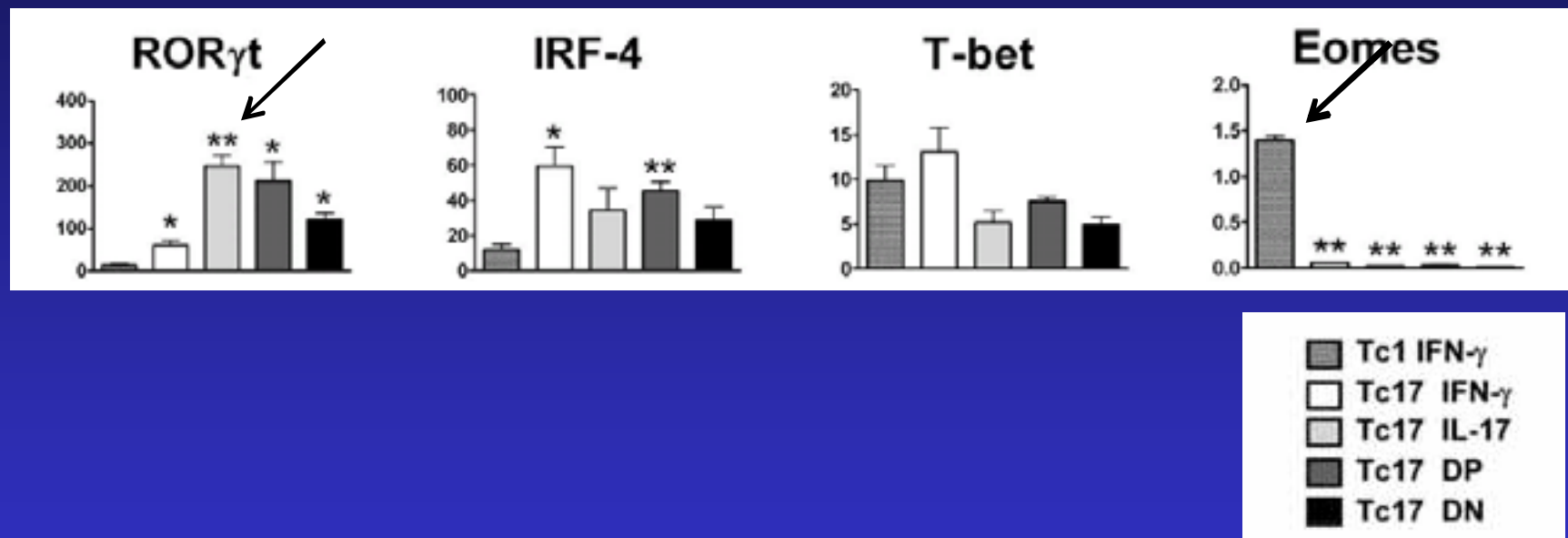
Sorting by Cytokine Secretion



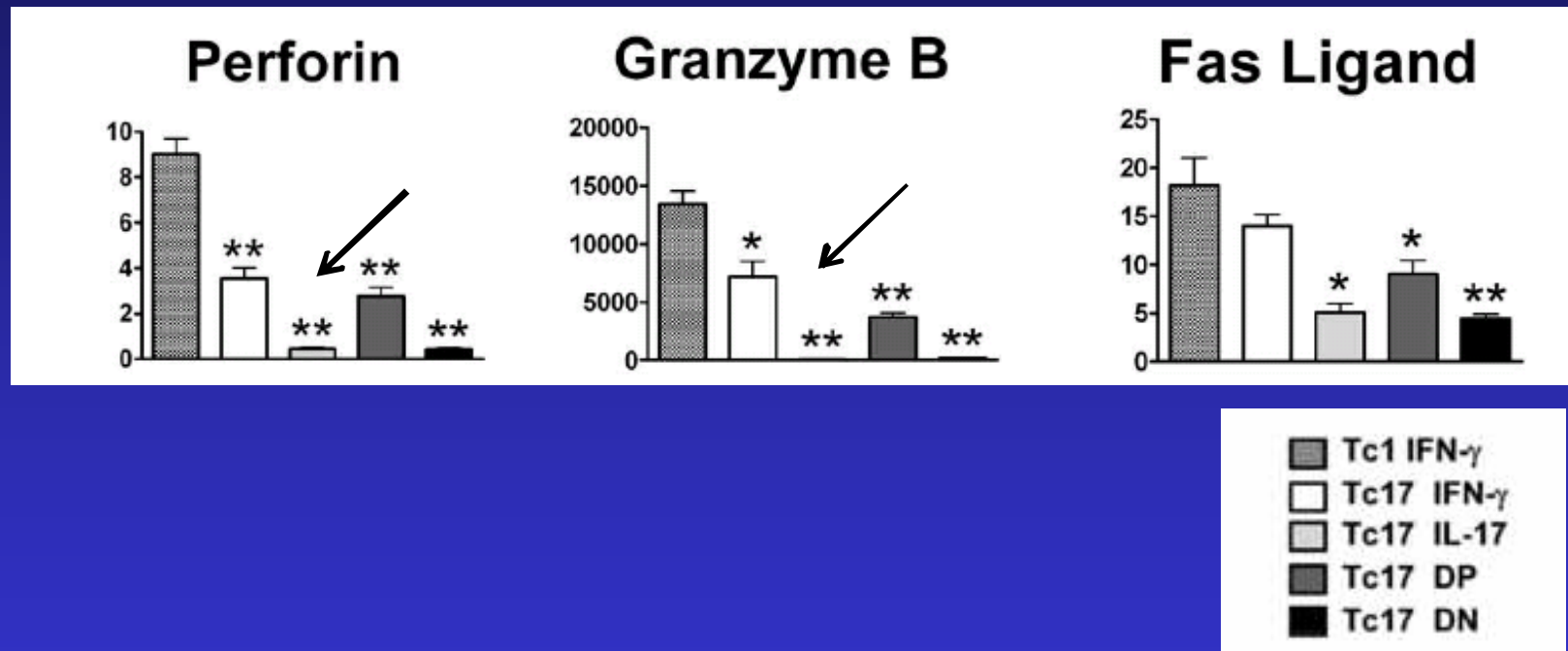
qPCR Analysis: Sorted Tc17 vs.Tc1 CD8 Cells (cytokines)



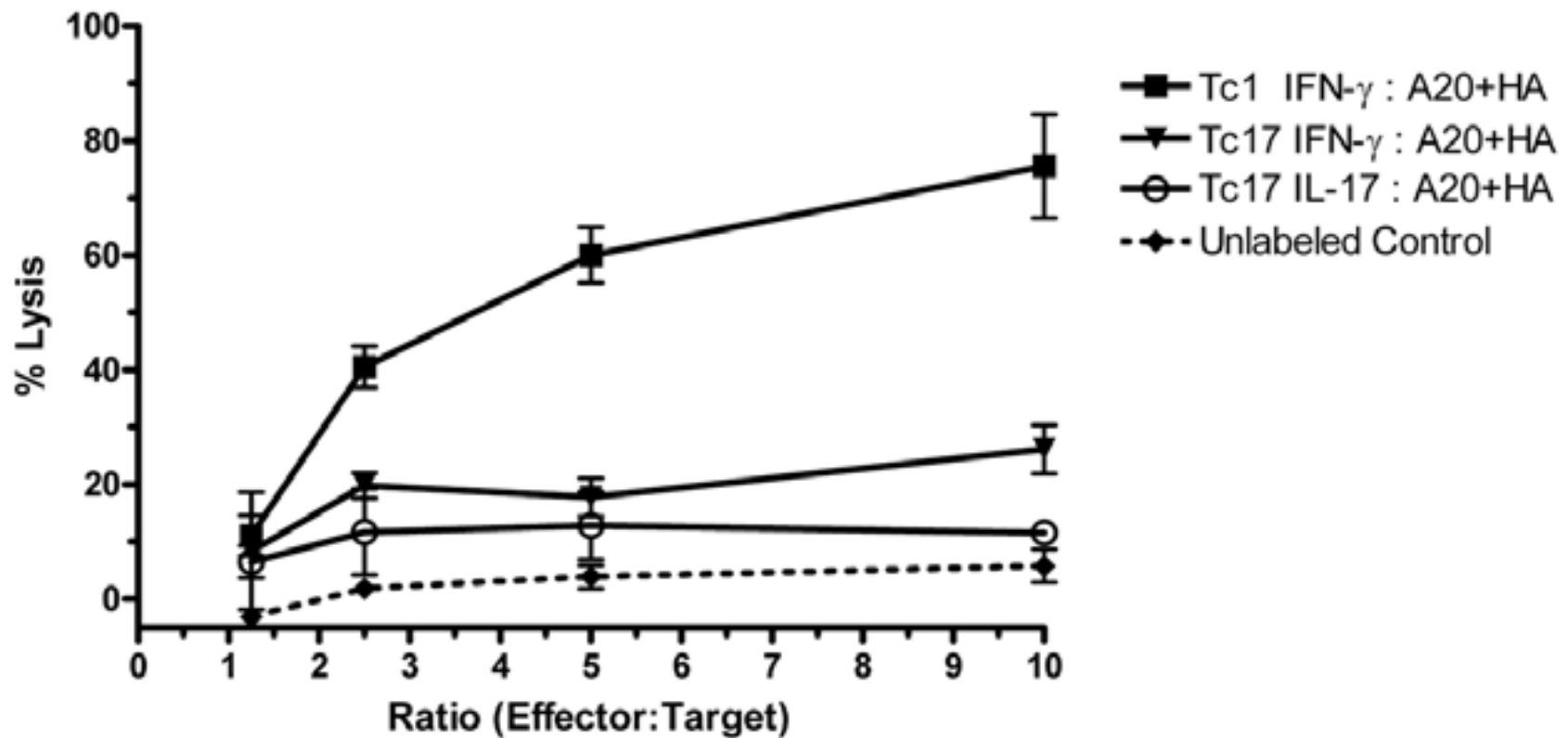
qPCR Analysis: Sorted Tc17 vs.Tc1 CD8 Cells (transcription factors)



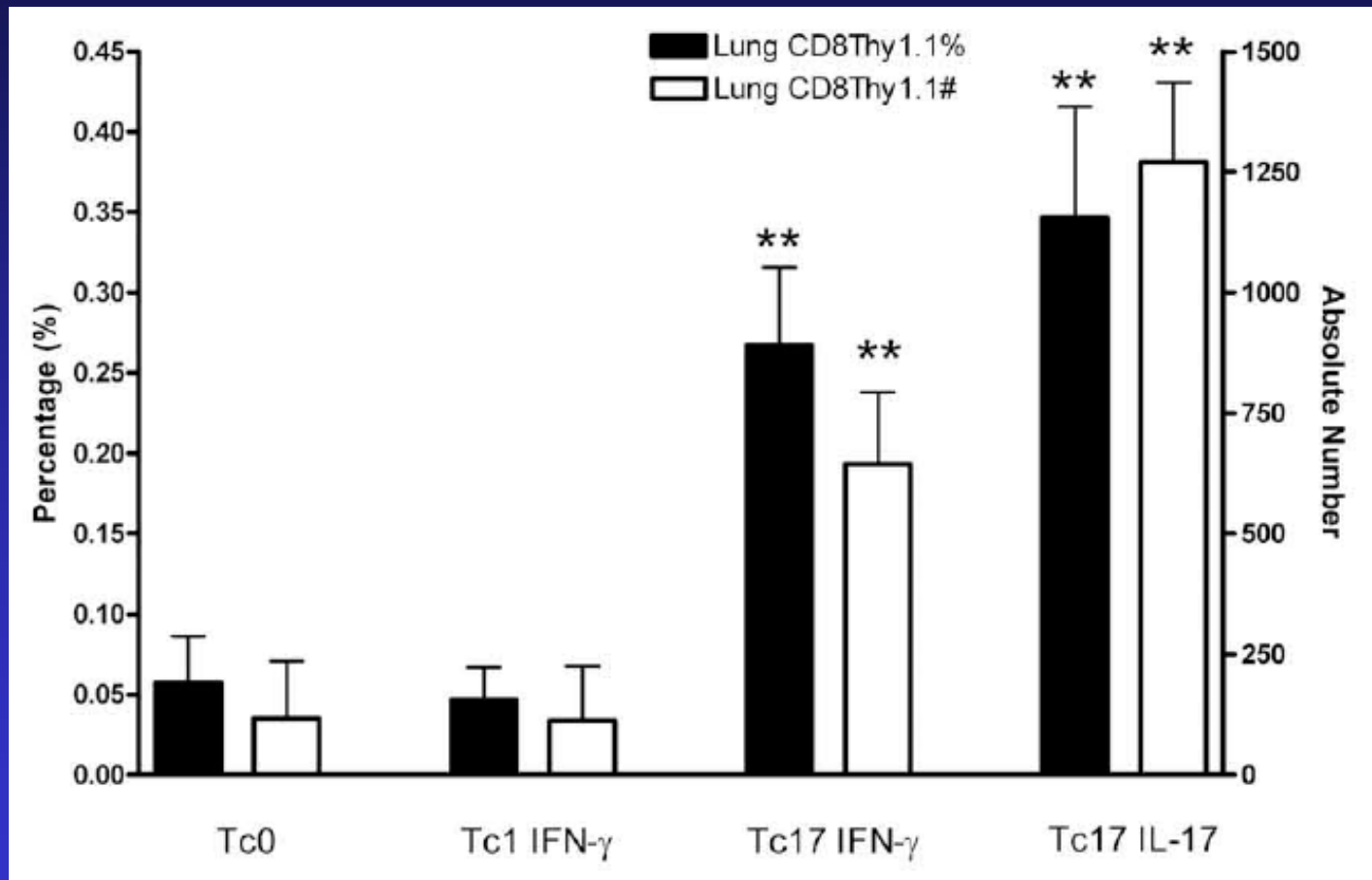
qPCR Analysis: Sorted Tc17 vs.Tc1 CD8 Cells (Effector Molecules)



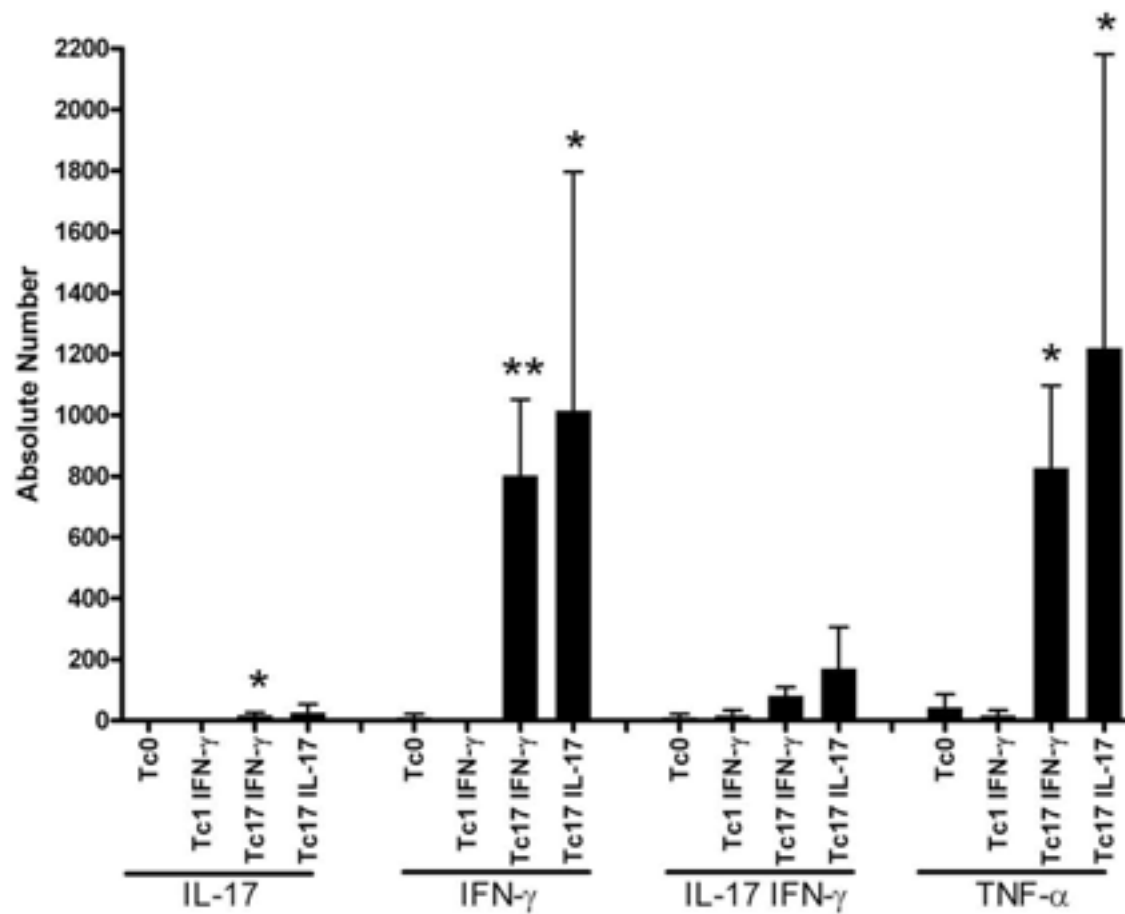
In VITRO – Tc17 are Non-Functional



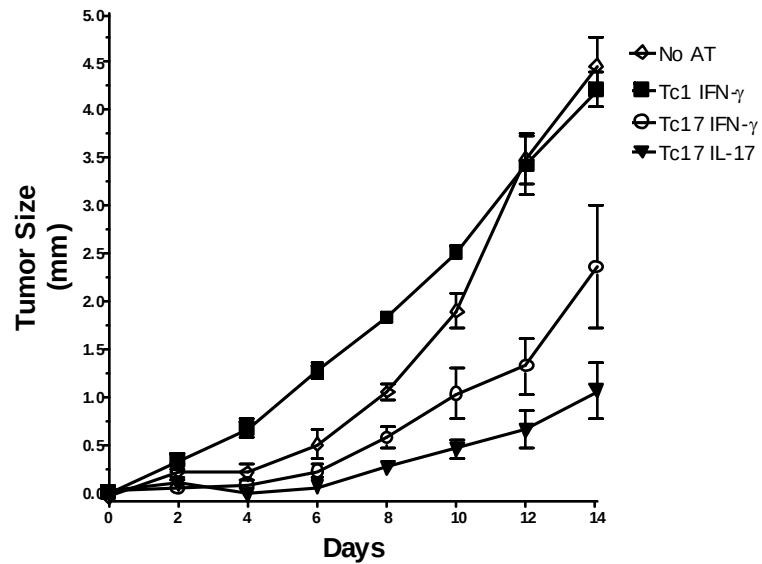
Adoptive Transfer of Specific Tc17: Lung Self-Antigen Model



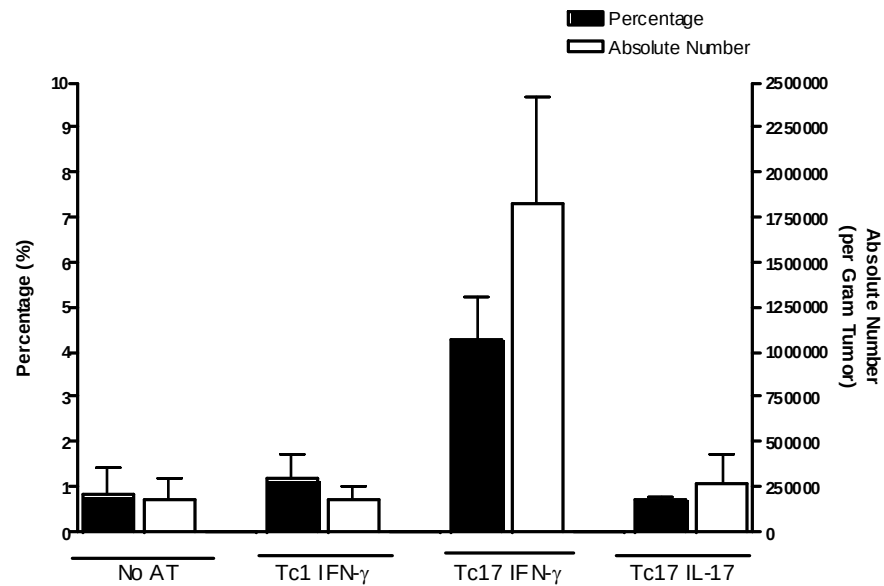
In Vivo Conversion of Tc17: From IL-17 Secretion to IFN- γ



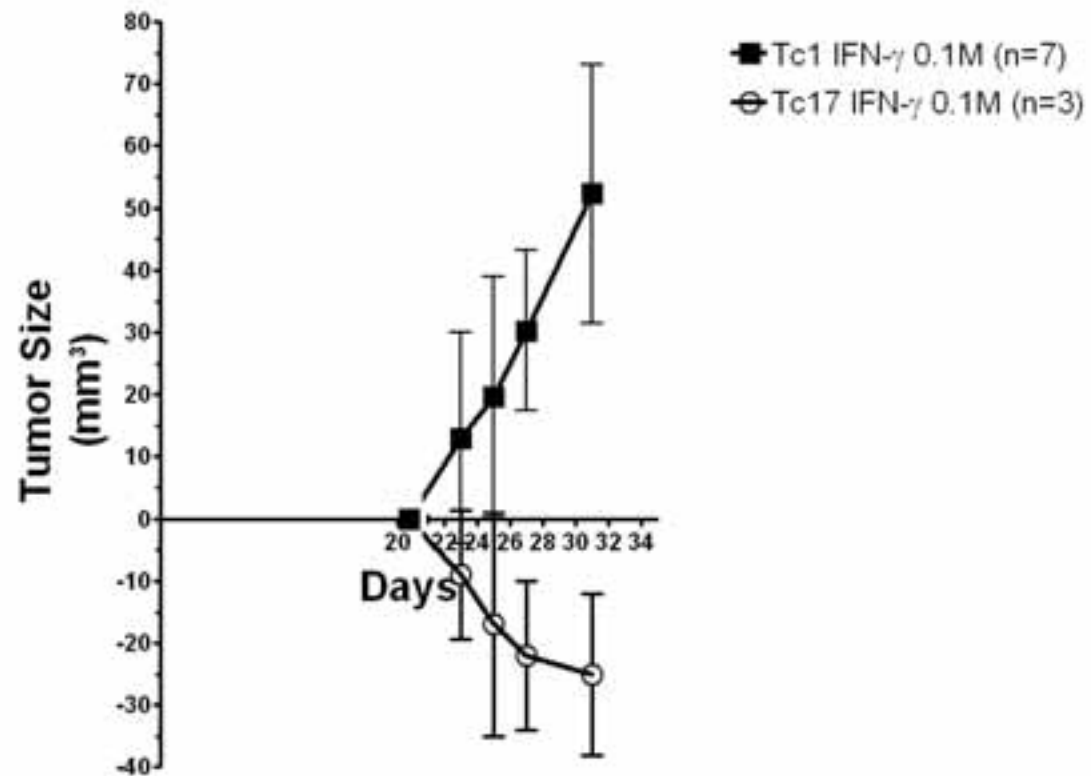
ISBT C



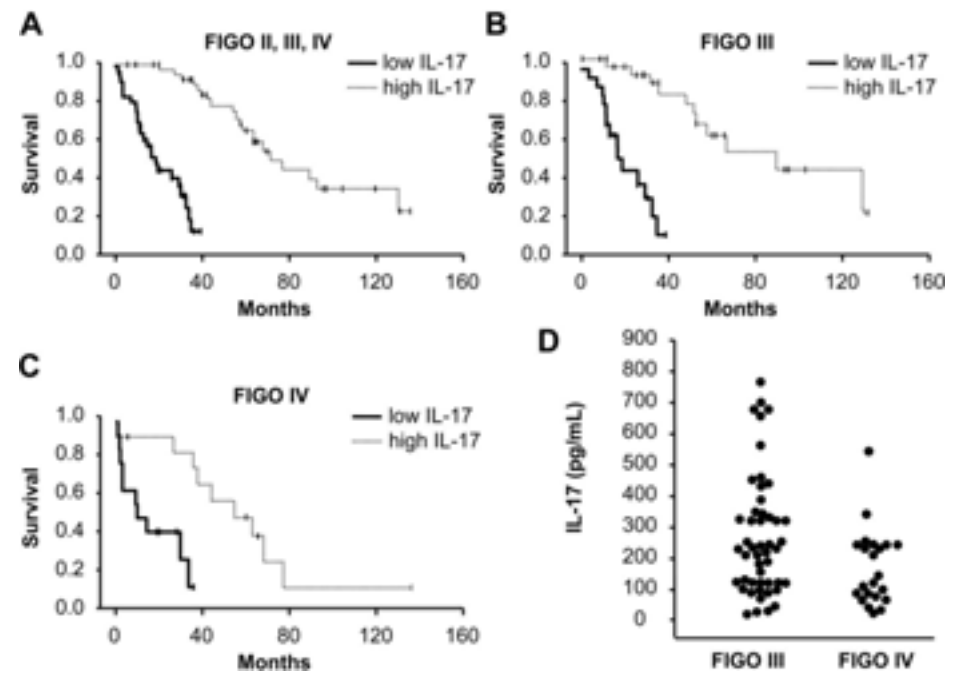
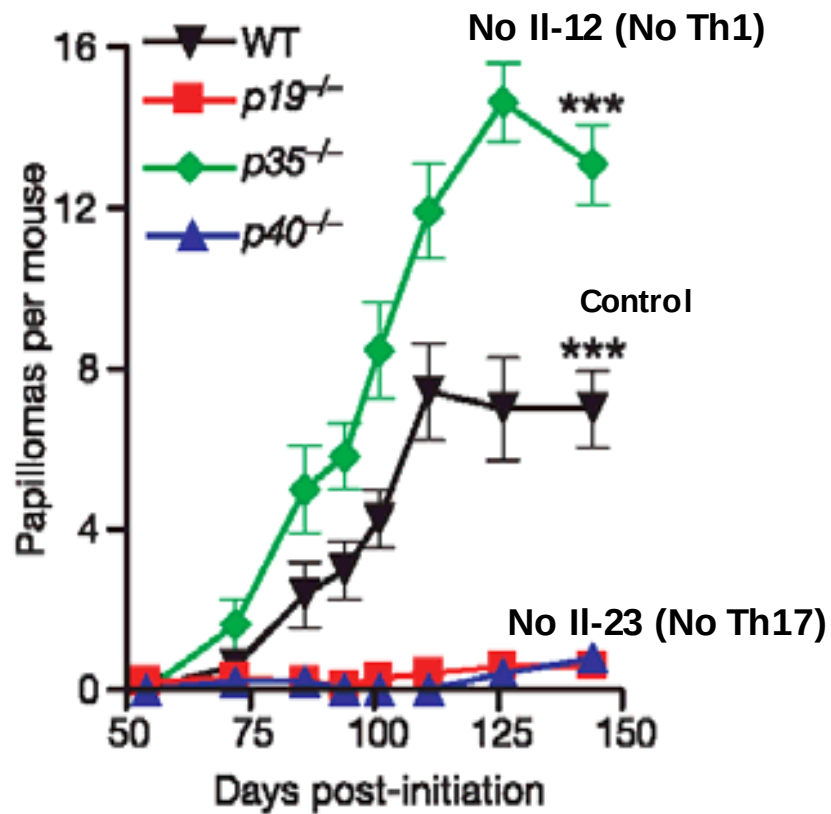
CT-26 HA Colon Tumor Model



MMTV-neu Treatment Model



IL-17 OR



Summary

1. CD8 as a source of IL-17
(Importance in vivo?)
2. TC17 Conversion to IFN γ Secretion in Vivo
Self-Antigen Model (pathology)
Tumor Antigen Model(s) treatment
Quantity versus quality?
3. IL-17 in tumor microenvironment
Other cell sources
Association with prognosis

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- Angelo De Marzo

MMTV-neu

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- Liz Jaffee