IL-17 Secreting CD8 T Cells (Tc17)

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Disclosure Of Financial Relationships

• Consulting:
  Amplimmune, Bristol Meyers Squibb, Dendreon, IRX, ProTox, Medarex

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• Stock Ownership
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  Amplimmune, Medarex
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

R. Schrieber et al.
Prostate Cancer: Treg Infiltration

Peripheral Blood Prostate

<table>
<thead>
<tr>
<th>FL4-H: FoxP3APC</th>
<th>SSC-H: Side Scatter</th>
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<tbody>
<tr>
<td>98.1</td>
<td>1.93</td>
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<tr>
<td>81.3</td>
<td>18.7</td>
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</tbody>
</table>

% CD4 T cells = FoxP3+

n=17  p<0.0001

K. Sfanos et. al. CCR 2009
Treg:
Correlation with Gleason Grade?

FoxP3

% Ratio: Prostate/Peripheral blood

Gleason 6
Gleason 7-9

p=0.5560

K. Sfanos et. al. CCR 2009
Prostate Cancer:
TH17 Infiltration

K. Sfanos et al. CCR 2009
$T_{H17}$: Correlation with Gleason Grade?

K. Sfanos et. al. CCR 2009
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 ?

Hung Rong Yen – JI (In Press)
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
(Effectector 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

![Graph showing tumor size over days for different treatments. The graph includes data points for Tc1 IFN-γ 0.1M (n=7) and Tc17 IFN-γ 0.1M (n=3).]
Il-17
OR

Langowski, J. et. al.
Nature 442:461, 2006

Kryczek I. et. al.
Blood 114:1134, 2009
Summary

1. CD8 as a source of IL-17
   (Importance in vivo?)

2. TC17 Conversion to IFNγ 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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