Biomarkers from the Tumor Microenvironment: Are they Useful?

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Biomarkers from the tumor microenvironment

• Tumor microenvironment events affect tumor outcome
• Tumor microenvironment events are identifiable through cellular or molecular markers
• Markers are mechanistically relevant
• Modulation of tumor microenvironment affects tumor outcome
• Modulation of tumor microenvironment can be traced through these markers
Tumor Microenvironment

Cancer Cells

Cancer Cell: Stroma Cells

Immune Cells

Endothelial Cells

The Reductionist View

A Heterotypic Cell Biology
Do Leukocytes Play a Role in Ovarian Cancer?

Cellular Biomarkers
- Intratumoral T cells
- T regulatory cells
- Vascular leukocytes
Intratumoral T cells

CD3+

54.8%

38.7%

6.5%

N=174

Zhang et al., *NEJM* 2003
Impact of TILs on Outcome in Ovarian Cancer
Stage III/IV – All patients (n=174)

Zhang et al., NEJM 2003
TILs correlate with tumor-reactive PBLs

<table>
<thead>
<tr>
<th>Patient No.</th>
<th>ELISPOT</th>
<th>TILs</th>
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<tbody>
<tr>
<td>OV22</td>
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<td>+</td>
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<tr>
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<tr>
<td>OV34</td>
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$P < 0.045$
Intratumoral T cells exhibit oligoclonal expansion
TILs Recognize TAAs in Ovarian Cancer

Bob Vonderheide
Proposed Biomarkers for Tumor Immune Surveillance

- Intratumoral CD8$^+$ T cells
- IFN-γ, MIG, IP-10
- pLCK, pZap-70
- NKG2D ligands
**CD4^+CD25^+ Treg**

![Flow cytometry plots](CD8_CD4_CD45_R3_R3.png)

Woo et al., *Cancer Res* 2002; *J Immunol* 2003
Regulatory CD4^+CD25^+ T Cells in Ovarian Cancer

Proposed Biomarkers for Tolerance

- CD4^+CD25^+ T cells
- foxP3
- GITR, CTLA-4
- Neuropilin-1
- IL-10, TGF-β
- PD-1
**Vascular Leukocytes**

CD11c+ cells with DC / endothelial phenotype and vasculogenic competence

Conejo-Garcia et al., Nature Med 2004
Endothelial cells and vascular leukocytes coexist in human ovarian cancer

Conejo-Garcia et al., *Blood* 2004
Proposed Biomarkers for Angiogenesis

- CD45$^+$CD11c$^+$VE-cadherin$^+$ cells
- VEGF-A
Activity of Biological Therapy in Ovarian Cancer

- Conejo-Garcia et al. *Nat Med*. 2004
- Hodi et al., *PNAS* 2003
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