Overcoming immune suppression/tolerance in cancer patients

Thomas F. Gajewski and Elizabeth M. Jaffey
Tumor escape from immune response: *priming phase* or *effector phase*?
New focus on downstream defects in effector phase of immune response in tumor microenvironment

Lymph node

- nCD8
- IL-2
- eCD8

Blood

Lymphatic

Tumor site

- APC
- Granzymes
- IFN-γ
- eCD8
Complexity of suppressive mechanisms in melanoma microenvironment

Ex vivo TIL dysfunction

Absence of B7 costimulation

Presence of FoxP3

Expression of IDO
Uncoupling negative regulation to improve immune-mediated tumor rejection

- **Homeostatic proliferation**
  - Maintains T cell function and reverses anergy
- **Stroma destruction**
  - Eliminates support structure
  - Perhaps eliminates myeloid suppressor cells
- **IDO inhibition**
- **Regulatory cell depletion**