Tumor Immune Escape:
Clinical Observations

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Tumor Immunotherapy: Immune Escape

‘Manipulated’ vs ‘Endogenous’

- Vaccine
- Adoptive T Cell Therapy
- Innate
- Adaptive
Tumor Immune Surveillance

Innate Immunity

Normal → Tumor

NK

NKT

IEL

IFN-γ + CK

DC

mφ

NK

NKT
Tumor Immune Surveillance

Adaptive Immunity

Normal

Tumor

CD8

CD4

DC
Immunoediting and Immunoselection

Genetic instability / Tumor heterogeneity

Selection and Expansion of Tumor variants

Natural Selection

Effective Immunotherapy

Genetic instability, Selection & Expansion
TUMOR CELL - ASSOCIATED

Antigen Processing/Presentation

Inhibitors of Apoptosis

Counterattack
ACCESSORY CELL - ASSOCIATED

T Cells

Apoptosis

Kynurenines

Tryptophan

IDO

Dendritic Cells

Regulatory T Cells

Gr-1

Suppressor cells

Arg Depletion

NO ONOO-

TGF-β

IL-10 TGF-β

CTLA-4

? IL-13, IL-4
Mechanistic Considerations of Tumor Immune Escape

- What makes a tumor site uniquely immunosuppressive?
- Interplay among different regulatory mechanisms and immune cells
Tumor Immune Surveillance

Adaptive Immunity

Normal

Tumor

Effector

Afferent
Mechanistic Considerations of Tumor Immune Escape

- What makes a tumor site uniquely immunosuppressive?

- Interplay among different regulatory mechanisms and immune cells

- Models to identify novel mechanisms of immune escape and evaluate potential solutions?
Translational Considerations for Evaluating and Overcoming Tumor Immune Escape

- Do these mechanisms exist in vivo?
- Relevance in subverting a clinical response?
- Availability of tools to monitor immune escape?
- Design of clinical trials to monitor and evaluate these factors?
- Interventions - reagents or strategies?
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