Cancer Immunotherapy

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What is Cancer Immunotherapy?

- Treatment that uses certain parts of a person’s immune system to fight diseases such as cancer.

Immunotherapy = T cell kills a cancer cell
How Does Immunotherapy Work?

• **Stimulate a person’s immune system to work harder or smarter** to attack cancer cells

• **Give a person immune system components**, such as man-made immune system proteins

- American Cancer Society
Various Classes of Immunotherapeutic Agents

Cytokine Therapy
- IL-2, IFN
- IL-7, IL-15, IL-21

Checkpoint blockade
- anti-CLTA4
- anti-PD1

Tumor-specific T cell

Tumor cell

T cell clones

CAR T cells

TCR engineered T cells

Therapeutic Vaccines
- Dendritic cell vaccines
- DNA, RNA, Engineered tumor cells

Chemotherapy
- T_reg
- MDSC

Antibody-drug conjugates
- Gentuzumab ozogamicin

Native antigen
Tumor-Derived Immune Suppression

Immunosuppressive Molecules (PD-L1)

Immunosuppressive Enzyme Activity
Indoleamine 2,3 Dioxygenase (IDO)

Immunosuppressive Cytokines
- TGF-β
- IL-4
- IL-6
- IL-10

Antigen Downregulation
Class I MHC loss in tumor cells

Positive and Negative Signals Regulate T-Cell Activation
“Driving” an Immune Response

T-cell receptor: Antigen-MHC

CD28: B7

CTLA-4: B7

Vaccine?
Ipilimumab Augments the Activation of the T-Cell

**T-cell activation**

- T-cell
- CD28
- CD80/CD86
- TCR
- HLA
- APC

**T-cell inhibition**

- T-cell
- CD28
- CTLA-4
- TCR
- HLA
- APC

**T-cell remains active**

- T-cell
- CD80/CD86
- TCR
- HLA
- APC

*Ipilimumab prevents CTLA-4 from inhibiting T cell activation*
How do Anti-PD-1/PD-L1 Antibodies work?

Tumor Microenvironment
Tumors Responsive to (Approved for) PD1/PD-L1 Blockade

- Melanoma
- RCC
- NSCLC
- Bladder (Urothelial)
- Head & Neck Squamous Cell Cancer
- Merkel Cell
- Hodgkin’s Disease
- Gastro-Esophageal
- Hepatocellular
- Mismatch Repair Deficient Tumors
Adoptive Cellular Therapy
Antibodies can act to target cytotoxic and toxic drugs, radioisotopes, immune cytokines, and immune effector cells to sites of tumor. Antibodies can be modified from a foreign mouse protein (antibody) to a completely humanized antibody. This may decrease their immunogenicity and improve function.
Tumor Vaccines

1. Whole Tumor Cell Vaccines
2. Peptide Vaccines from tumor associated proteins (TAA)
3. DNA Vaccines – isolated tumor DNA
4. Dendritic Cell (DC) Vaccines pulsed with peptides (TAA)
5. DC Vaccines into tumors
Questions?
Ask the Experts!