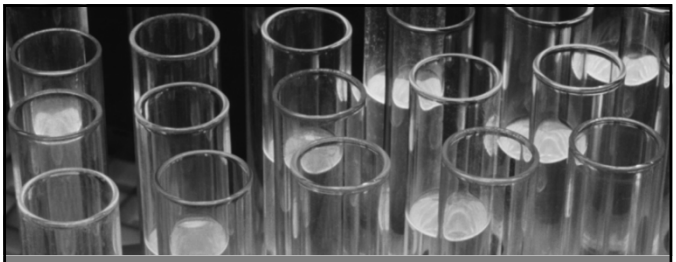

Immunotherapy

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Conflict of Interest Statement

I have no conflict of interest to disclose and no financial or other interest associated with patient privacy or any entity that has a pecuniary or tangible interest in patient privacy or the use of patient information for gain of any kind.

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Immunotherapy Learning Objectives

- Discuss history of immunotherapy
- Identify at least two types of immunotherapy
- Describe common side effects associated with immunotherapy
- Name one famous person associated with immunotherapy

Immunotherapy Theory……..

- Works to boost the immune system to attack the cancer
- Cancer cells can hide from the immune system: multiple techniques…..
- Cancer cells trick the immune system
- Potential to remain effective long after end of treatment

History of Immunotherapy

- It all began in 1890…..
  - Dr. William Coley
    - Coley's Toxins
- 1956:
  - Tumor-specific cell antigens discovered
- 1984:
  - Society for Immunotherapy of Cancer founded
- 2014:
  - Nivolumab (Opdivo) & Pembrolizumab (Keytruda), approved for advanced melanoma

Types of Immunotherapy

- Nonspecific Immune Stimulation
- T-Cell Therapy
- Immune Checkpoint Inhibitors
- Cancer Vaccines
- Monoclonal Antibodies
- Oncolytic Virus

Nonspecific Immune Stimulation

- Strategy that gives the immune system a boost
- Types:
  - Cytokine
    - Interleukins
    - Interferons
    - Granulocyte-macrophage-colony stimulating factor (GM-CSF)
  - Modified Bacteria
    - Ex. BCG (Bacillus Calmette Guerin)
  - Toll-like receptor agonists

Adoptive T-Cell Therapy

- Involves enhancing the body's own T-cells to fight cancer:

  1) tumor-infiltrating lymphocytes

  2) chimeric antigen receptor T-cells (CAR-T)
- T-cells multiply, seek, and destroy the cancer cells
- Only available through clinical trials

Immune Checkpoint Inhibitors

- Blocks the checkpoint from being engaged → Turns the immune response back on
- Types:
  - Anti-CTLA-4 antibodies
    - Tremelimumab
    - Ipilimumab
  - Anti-PD-1 drugs
    - Nivolumab
    - Pembrolizumab
  - Anti-PD-L1 molecules
    - Avelumab
    - Durvalumab
    - Atezolizumab

Immunotherapy Video Demonstration

Immunotherapy: How the Immune System Fights Cancer

https://www.youtube.com/watch?v=jDdL2bMQXfE

- Non-Specific Immune Treatment
- T-Cell Therapy
- Immune Checkpoint Inhibitors

Cancer Vaccines

- Prophylactic: HPV & HBV
- Therapeutic:
  - Can be developed from patient's own tumor
  - Usually "off-the-shelf"
    - 1 to 100 antigens common to type of cancer
- Types:
  - Tumor cell vaccines
  - Antigen vaccines
  - Dendritic cell
  - Vector-based vaccine

Monoclonal Antibodies

- Antibodies designed to target specific tumor antigens (mAbs)
  - Flagging, blocking, delivering
  - Carry drugs, particles, proteins directly to cancer cells
- 3 Different Types:
  - Naked mAbs
  - Conjugated mAbs
  - Bispecific mAbs

Oncolytic Virus

- Uses viruses to attack the cancer cells
- Only 1 approved by FDA
  - Herpes-simplex virus contains GM-CSF, drug called T-VEC
    - Melanoma
- Duke University (Tisch Brain Tumor Center)
  - Poliovirus therapy for recurrent GBM
    - Polio to treat cancer? 60 minutes report aired 3/29/15

Common Side Effects

- Fatigue
- Mild Skin
- Diarrhea
- Flu-like Symptoms
- Immune-Mediated Adverse Reactions:
  - Endocrine, GI, Neurologic, Pulmonary, Renal, Severe Skin

Notable People & Immunotherapy

- Former President Jimmy Carter
  - “I want what he had”…….
  - Type of Cancer: Melanoma
- 2018 Nobel Prize for Physiology or Medicine
  - James Allison: in 1980s identified CTLA-4 on T cell receptors
  - Tasuku Honjo: in 1992 identified PD-1 on T cell receptors

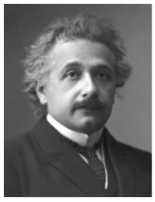
Clinical Trials

- Phase I, II, & III
- Immunotherapy: alone & combined with SOC
  - www.clinicaltrials.gov
- Eligibility Requirements: specific for each trial
  - Type of Cancer
  - Previous Treatment
  - ECOG status
  - Tumor Burden

Research is Promising…..

"If we knew what we were doing, it wouldn't be called research, would it?"

~Albert Einstein



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