Cancer immunology is the study of how the **immune system interacts with cancer**—both in recognizing and eliminating tumor cells, and in how tumors evade immune responses. It forms the foundation of modern **immunotherapies**, which aim to harness the immune system to treat cancer.

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□ Key Concepts in Cancer Immunology

1. **Immunosurveillance** - The immune system constantly scans for abnormal cells. - Tumor cells can be destroyed before they form detectable cancers. - This process involves **cytotoxic T cells**, **NK cells**, and **macrophages**.

2. **Immunoediting** This is a dynamic process in three phases: - **Elimination**: Immune system destroys tumor cells. - **Equilibrium**: Some tumor cells survive but are kept in check. - **Escape**: Tumors evolve to **evade immune detection** and grow uncontrollably.

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□ Key Players

- **Cytotoxic CD8+ T cells**: Kill tumor cells directly. - **Helper CD4+ T cells**: Support immune response via cytokine release. - **Regulatory T cells (Tregs)**: Suppress anti-tumor immunity (often hijacked by tumors). - **Tumor-associated macrophages (TAMs)**: Can promote or suppress tumor growth. - **Myeloid-derived suppressor cells (MDSCs)**: Inhibit T cell responses. - **Dendritic cells (DCs)**: Present tumor antigens to T cells.

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□ Tumor Immune Evasion Strategies

- **Downregulating MHC class I** to avoid T cell recognition - **Expressing immune checkpoint ligands** (e.g., PD-L1) to turn off T cells - **Creating an immunosuppressive microenvironment** (e.g., via TGF-β, IL-10) - **Recruiting Tregs and MDSCs** to suppress immunity - **Shedding antigens** or **mutating** to avoid immune recognition

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□ Immunotherapy Approaches

1. **Checkpoint inhibitors**

    1. Block inhibitory signals like **PD-1/PD-L1** and **CTLA-4**
    2. Boost T cell activity (e.g., nivolumab, pembrolizumab)

2. **CAR-T cell therapy**

    1. T cells engineered to express **chimeric antigen receptors** targeting specific cancer antigens (e.g., CD19 in B-cell malignancies)

3. **Cancer vaccines**

    1. Stimulate immune system to recognize tumor antigens

4. **Oncolytic viruses**

1. Viruses that selectively infect and kill tumor cells while activating immunity

5. **Cytokine therapies**

1. IL-2, IFN-α to boost immune responses (though with side effects)

6. **Bi-specific T cell engagers (BiTEs)**

1. Link T cells to cancer cells (e.g., blinatumomab)

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□ Current Research & Challenges

- **Tumor heterogeneity**: Different clones may escape immune detection. - **Immune-related adverse events (irAEs)** from overactivation of the immune system - **Non-responsive tumors**: “Cold tumors” that lack T cell infiltration - Development of **biomarkers** to predict response to therapy (e.g., PD-L1 expression, tumor mutational burden)

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□ Clinical Examples

- **Melanoma**: Among the first cancers successfully treated with checkpoint inhibitors - **Lung cancer**: Improved survival with PD-1/PD-L1 inhibitors - **Glioblastoma**: Immunotherapy is under investigation but faces immune privilege of the brain and a suppressive microenvironment

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□ Take-home Message

Cancer immunology reveals the **complex battle between tumors and the immune system**. By understanding and manipulating this interaction, **immunotherapy has revolutionized oncology**, especially for cancers once considered untreatable.