Nibs, Nabs, Mibs & Mabs
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NORMAL CELLS
- Respects Anti-growth Signals
- Respects Boundaries
- Fixed Number of Replications
- Appropriate Growth Signal Responses
- Normal Metabolism
- Respects Apoptosis Signals
- Active Replication Checkpoints

CANCER CELLS
- Ignores Anti-growth Signals
- Sustained Proliferation
- Invades and Metastasizes
- Hyperactive Metabolism
- Broken Replication Checkpoints
- Evades Immune System
- Unlimited Replications
- Escapes Apoptotic Signals
- Sustained Angiogenesis
- Evades Immune System
- Hyperactive Metabolism

CHEMOTHERAPY
TARGETED THERAPY
Targeted Therapy vs Chemotherapy

**CHEMOTHERAPY**
- Acts on all rapidly dividing normal and cancerous cells
- Compounds identified because they kill cells
- Cytotoxic - they kill tumor cells

**TARGETED THERAPIES**
- Act on specific molecular targets that are associated with cancer
- Compounds deliberately chosen or designed to interact with their target
- Cytostatic - they block tumor cell proliferation

Chemotherapy

Chemotherapy works by stopping or slowing the growth of cells which grow and divide quickly.

Chemotherapy is used to:
- **Treat Cancer**: cure cancer, lessen the chance it will return, or stop or slow its growth.
- **Palliative care**: Shrink tumors that are causing pain and other problems.
- **Neoadjuvant chemotherapy**: Make a tumor smaller before surgery or radiation therapy.
- **Adjuvant chemotherapy**: Destroy cancer cells that may remain after treatment with surgery or radiation therapy.
- **Help other treatments work better.**

Targeted Cancer Therapy

Targeted drugs zero in on some of the changes that make cancer cells different. They target specific areas of the cancer cell that allow the cell to grow faster and abnormally. There are many different targets on cancer cells and many drugs that have been developed to attack them.

In general targeted drugs work to:
- Block or turn off chemical signals that tell the cancer cell to grow and divide
- Change proteins within the cancer cells so the cells die
- Stop making new blood vessels to feed the cancer cells
- Trigger your immune system to kill the cancer cells
- Carry a toxin to the cancer cell to kill it, but not normal cells

Our understanding of cell biology was at one time as simple as this...
Our current knowledge now reveals a tangled web of signaling

For cells to function normally, complex communication systems govern basic cellular functions:
• Cell division (proliferation)
• Cell migration
• Response to external stimuli
• Cell death (apoptosis)

Goals of targeted therapy
• Find pathway unique to cancer
• Develop mechanism to switch pathway “off”

Extra- & Intracellular Signaling

• Cells communicate with each other by secreting signals (ligands) which can be proteins or other molecules.
• In order to detect a signal (that is, to be a target cell), a neighbor cell must have the right receptor for that signal.
• When a signaling molecule binds to its receptor, it alters the shape or activity of the receptor, triggering a change inside of the cell.
Types of Targeted Therapies

Nibs: Small Molecule Kinase Inhibitors

- Erlotinib

GREEN – Epidermal Growth Factor
RED – ATP binding site

ATP

Types of Targeted Therapies

Nabs: Nanoparticle, Albumin-bound

- Allows for non-toxic delivery of hydrophobic therapeutic compounds.
- Exploits the natural properties of albumin. Albumin reversibly binds to and transports a wide range of molecules from the bloodstream to cells.
- Once the Nab-drug combo enter the interstitial space, the drug “payload” is released from the albumin.
- The cytotoxic drug then diffuses into the tumor cells where it induces apoptosis.

Types of Targeted Therapies

Mibs: Proteosome Inhibitors

- CARFILZOMIB

- The proteosome is responsible for the digestion of proteins inside the cell.
- If proteosome function is blocked, the build-up of these proteins triggers apoptosis.

Types of Targeted Therapies

mAbs: Monoclonal Antibodies

A. Direct signaling induced death of cancer cells (e.g. herceptin and rituximab).
B. Inhibit angiogenesis (e.g. bevacizumab)
C. Block inhibitory signals thereby resulting in a stronger anti-tumor T cell response (e.g. ipilimumab and nivolumab)
D. Deliver radionuclides (e.g. 131I tositumomab)
E. Deliver highly potent toxic drugs directly to cancer cells (trastuzumab emtansine)
F. Retarget immune cells towards cancer cells with special mAb that connects the two (e.g. blinatumomab)
G. CAR T-cells
Types of Targeted Therapies
mAbs: Monoclonal Antibodies

A Partial View of Immune System Regulators

Immun checkpoint inhibitors are a hot area of clinical research.

Questions?
Comments?

THANK YOU!!