Tumor immunology

Immune surveillance

Definition: Daily screening of all body cells by I.S to recognize and destroy any altered (tumor) cell.

Which cells involved in immune surveillance?

1- NK cells

2- Cytotoxic T cells

3- Macrophages

What are the evidence that immune responses occur against tumor cells?

- Immunosuppressed patients – AIDS with Kaposi sarcoma
- Old age with increase frequency of tumors
- Both antibodies and T lymphocytes were detected in tumors
- Immunization against some tumors (HBV vaccine will reduce HCC cases

Tumor antigens

They are cell surface molecules on tumor cells and recognized by I.S.

Types of tumor Ags

1- Tumor specific Ags

2- Tumor associated Ags

1- Tumor specific Ags (Present only on tumor cells)

A- Oncogenic viruses transform host cells which express viral specific oncogenic antigens on their surfaces with MHC-1. Like HBV and HPV

B- Genetic mutation Like carcinogens, X rays which can transform host cells into cancer cells which express tumor specific antigen and not found in normal cells.

2- Tumor associated antigens

These Ags present in trace amounts in normal cells but increased in tumor (not unique to tumor cells)

Examples

A- Oncofetal antigens

(AFP=alpha feto protein antigen in liver carcinoma, CEA =carcinemberyonic antigen in colon cancer. These are present during emberyogenesis but decreased after puberty.

B- **HER2** in breast cancer

C- **PSA** in prostatic cancer

Immune responses against tumors

-Activation of T cytotoxic cells: tumor cells express tumor Ag on their surfaces by MHC-1---L.N

- **TH1 cell activation (APCs tumor Ag + MHC-II with secretion of IL-12. Activated TH1 cells secrete IL-2 (stimulate both NK cells and sensitized CD8 cells), INF-gamma (activate macrophages). TNF –necrosis of tumor cells**
- **TH2 cells activation----B cells activation---antibodies production that can kill tumor cells by opsonization, ADCC and complement activation**

But if such immune responses occur why tumor developed ?

Tumors can evade from immune responses

1- Immunosuppression (host) like AIDS patients who develop Kaposi sarcoma

2- Tumor cells release TGF-beta (immune suppression)

3- Tumor cells increase T reg cells which decrease T cell activation.

4- Tumor cells can make FasL and attack CD8 cells through Fas and kill them (Normally CD8 cells make FasL and bind with Fas on infected cells)

5- Tumor Ag too small to be detected by I.R (sneak through)

6- Lack of Ag (tumor cells don’t express surface Ag)

7- Antigenic shedding by tumors so humoral immune responses will generated against released Ags leaving tumor cell proliferating

8- Blocking antibodies. Even binding antibodies are non functional.

9- Reduction of MHC-I expression so no CD8 cell function

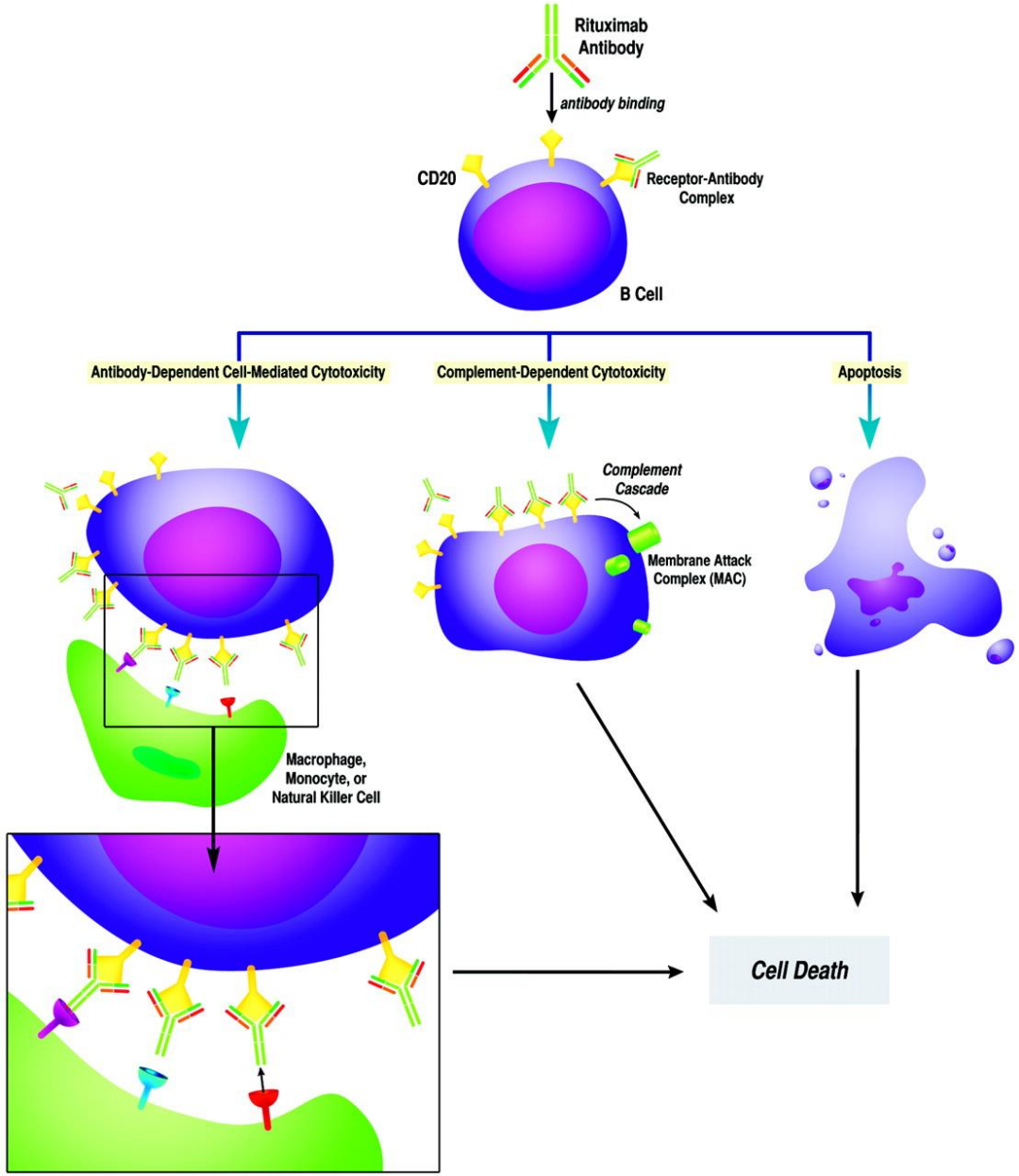
10- Lack of co-stimulatory signal . When APCs become tumor cells will no express B-7

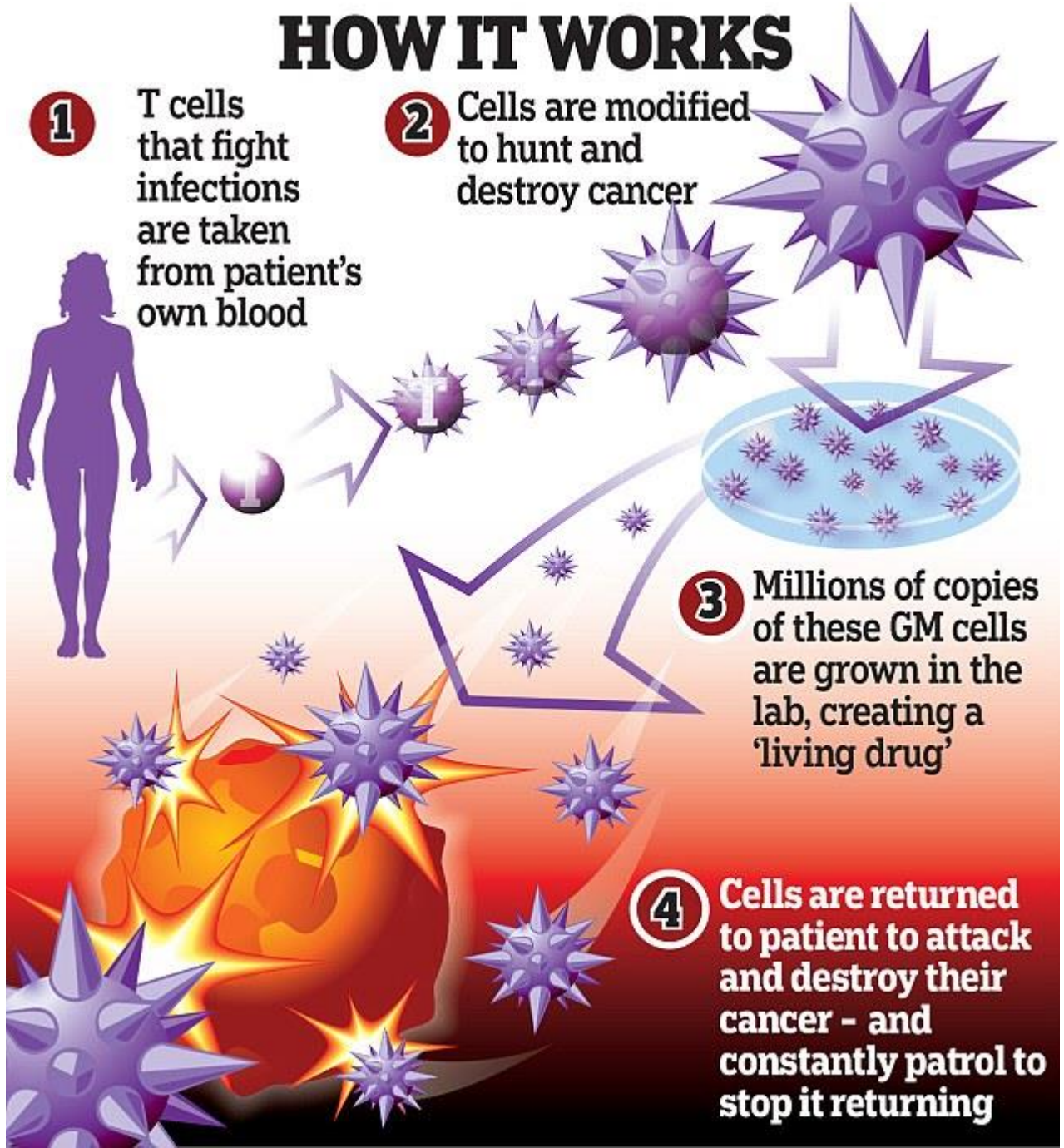
Tumor markers

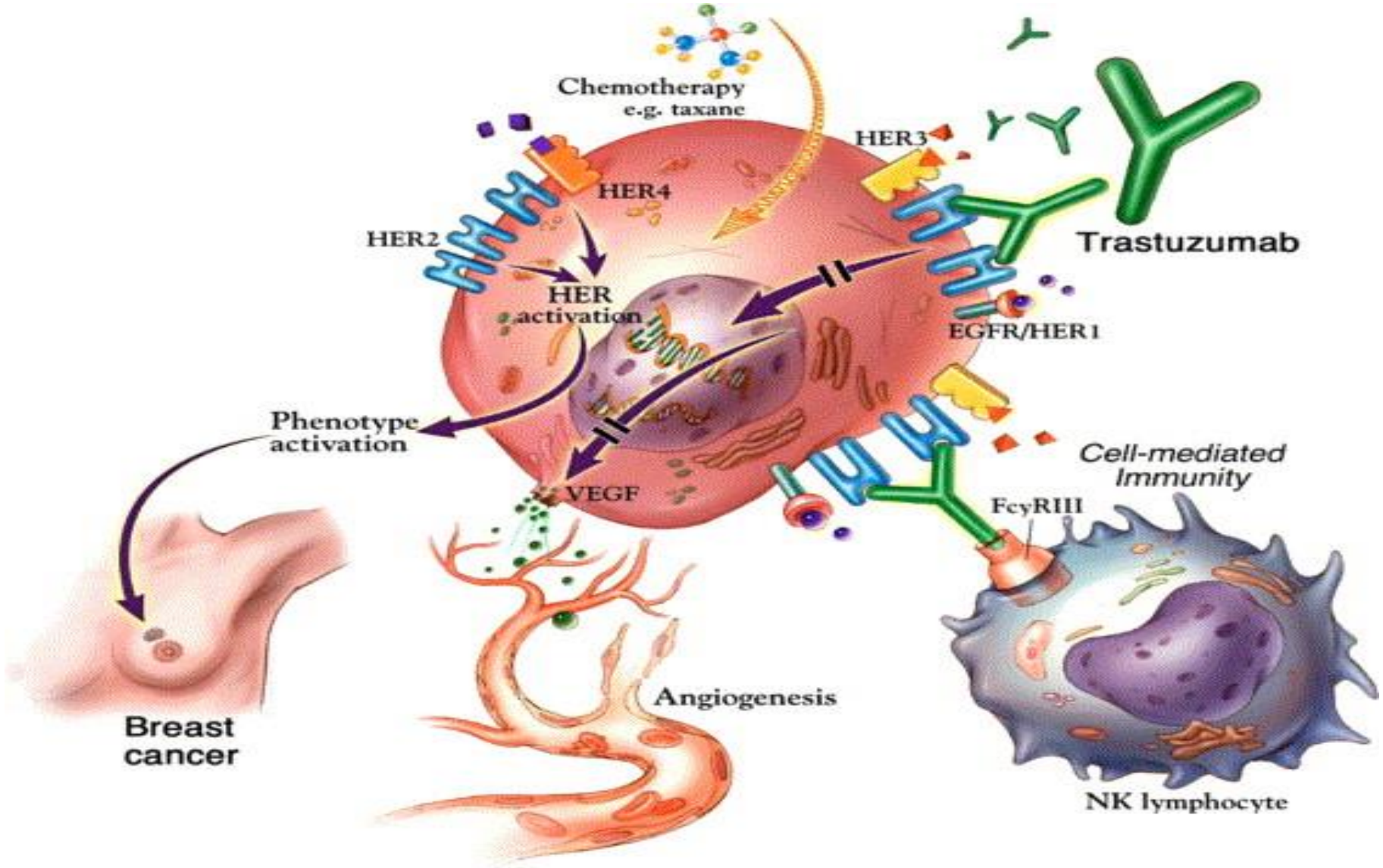
1- AFP--------liver carcimona (NR:0-20 ng/ml)
2- CEA------Colocancer (RR < 2.5 ng/m;
3- BHCG -----choriocarcinoma (cancer of placenta)
4- PSA---- Prostatic cancer
5- CA 125--- ovarian cancer
6- CA 19-9 ---- Pancreatic cancer
7- CA15-3 -------Breast cancer

Tumor immunotherapy
Biological therapy (Passive humoral immunotherapy like Herceptin) or using passive cellular immunotherapy by using activation NK cells or Lymphocytes from tumors then activation in the lab. By IL-2 then re-infused the same patient or combined therapy by combining cytotoxic drugs with specific monoclonal antibodies so antibodies will bind with tumor cell and cytotoxic drug and kill them.
Tumor cell vaccine

- Irradiated tumor cells + adjuvants-----injection
- Synthetic tumor peptide vaccine made from tumor antigen
- Tumoral viral vaccine like HBV vaccine to prevent HCC.


Rituximab
Antibody
antibody binding
CD20
Receptor-Antibody
Complex
B Cell
Antibody-Dependent Cell-Mediated Cytotoxicity
Complement-Dependent Cytotoxicity
Apoptosis
Complement
Cascade
Membrane Attack
Complex (MAC)
Macrophage,
Monocyte, or
Natural Killer Cell
Cell Death


HOW IT WORKS
1 T cells that fight infections are taken from patient's own blood
2 Cells are modified to hunt and destroy cancer
3 Millions of copies of these GM cells are grown in the lab, creating a 'living drug'
4 Cells are returned to patient to attack and destroy their cancer - and constantly patrol to stop it returning


Chemotherapy
e.g. taxane
HER3
HER4
HER2
Trastuzumab
HER
activation
EGFR/HER1
Phenotype
activation
Cell-mediated
Immunity
VEGF
FcγRIII
Angiogenesis
Breast
cancer
NK lymphocyte

Do you know?

- We want immune tolerance in case of organ transplantation to not be rejected.
- We do not want to be tolerance for tumors but unfortunately we are tolerant for them and finally they kill us without mercy.