

Immunity Against Tumors

Tumor, Neoplasm, Cancer

Introduction

- **Benign tumors:** Tumors in which cells remain clustered together at a single site.
- **Malignant tumors:** Tumors in which cells break off from the main tumor mass and be carried by the blood or lymph to distance sites and grow again.
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- **Carcinomas:** tumors arising from epithelial cells.
- Sarcomas: tumors arising from muscle, lymphoid or connective tissues.
- **Leukemia:** is a tumor derived from hemopoietic cells.
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- 1-Allograft individuals that exposed for longtime to immune-suppressers may develop tumor.
- 2-Individuals with congenital or acquired immunodeficiency syndroms develop tumor.

Tumor-associated antigens

- Tumor cells may show the followings:
- 1-They may lose MHC or blood group antigens.
- 2-They may produce tumor antigens known as oncofetal antigens (These ags are normally present in the fetus, like carcinoemryonic antigen).
- 3-They may produce α -fetoprotein by hepatoma cells.
- 4-They may produce antigenic mucins.
- 5-They may produce normal Ags in unusual quantities.
- 6-Some tumors induced by oncogenic viruses may produce antigens like FOCMA (Feline Oncornavirus Cell Membrane Antigen).

Immunity To Tumor

- If tumor cells are sufficiently different from normal cells, they will be regarded as foreign and attacked. The major mechanisms of tumor cell destruction involve:
 - A-ATTACK BY NATURAL KILLER (NK) CELLS.
 - B- ATTACK BY CYTOTOXIC T CELLS.
 - C- ATTACK BY ACTIVATED MACROPHAGES.
 - D- ANTIBODIES ARE ALSO PARTICIPATED.
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NATURAL KILLER (NK) CELLS.

- About 15% of peripheral blood lymphocytes are natural killer cells. They are characterized by their ability to kill tumor cells and virally infected cells. NK cells are large, granular, non-phagocytic lymphocytes. They are mainly found in the bone marrow, and non are found in the thymus.
- **Antigen Recognition**
- NK cells recognize tumor or other abnormal cells by a variety of mechanisms:
- NK cells will selectively kill target cells that fail to express MHC-class I molecules.
- NK cells can recognize a protein called MICA. This protein is not expressed on normal healthy cells, but is expressed on cancer cells and virus infected cells.
- NK cells also recognize target cells by an antibody dependent process.

Effector Mechanisms

- NK cells mediated killing is mediated, like T cells through perforines and cytotoxines (TNF- α and TNF- β). It produces characteristics small (5-7nm) lesions in target cells.
- Functions
- NK cells act as antitumor cells.
- Active against xenogenic virus infected cells.
- Active against bacteria like *Staphylococcus aureus* and *Salmonella typhimurium* and fungi.
- NK cells destroy cultured tumor cells in vitro.
- NK cells destroy human leukemia, myeloma and some sarcoma and carcinoma cells in vitro.

Regulation

- NK cells activity is regulated by IL-2, IL-3, IL-4, IL-12 and IFN- γ .
- IL-2 stimulates proliferation of NK cells.
- IL-3 prevent the death cultured NK cells.
- IL-4 stimulates NK function and enhance cytotoxicity.
- TNF- α and IL-12 produced by macrophages induce IFN- γ production by NK cells.
- IFN- γ enhances NK activity.
- NK cell function is also regulated by macrophage inflammatory protein (MIP) that attract NK cells to the site of tissue damage.

T CELL MEDIATED IMMUNITY

- 1-It is possible to detect cell-mediated response to tumor antigens either by skin testing or by use of an in vitro test such as macrophage migration inhibition.
- 2-Lymphocytes from some tumor bearing animals may exert a cytotoxic effect on tumor cells cultured in vitro.
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C-MACROPHAGE MEDIATED IMMUNITY

- In some experimental systems, macrophages may have an antitumor function. This is especially true of macrophages activated by exposure to IFN- γ . These activated macrophages release cytotoxic molecules such as arginase and reactive oxygen metabolites.

D-ANTIBODY MEDIATED IMMUNITY

- Antibodies to tumor cells are found in many tumor-bearing animals; for instance about 50 % of sera from dogs with lymphosarcoma contain precipitating antitumor antibodies. These antibodies may be of some protective significance since together with complement, they may lyse free tumor cells. Antibodies are not effective in destroying the cells in solid neoplasia.

FAILURE OF IMMUNITY TO TUMOR CELLS

- Mechanisms by which tumor escape immune defenses:
- 1) Reduced levels or absence of MHC I molecule on tumor so that they cannot be recognized by CTLs
- 2) Some tumors stop expressing the antigens
 - These tumors are called “antigen loss variants”
- 3) Production of immunosuppressive factors by tumor e.g. transforming growth factor (TGF- β)
- 4) Tumor antigens may induce specific immunologic tolerance
- 5) Tumor cells have an inherent defect in antigen processing and presentation
- 6) Blocking of receptors on T-cells by specific antigen antibodies complex (after shedding of tumor Ag) prevents them from recognizing and attacking tumor cells
- 7) Antigens on the surface of tumors may be masked by sialic acid-containing muco-polysaccharides
- 8) Immune suppression of the host as in transplant
 - patients who show a higher incidence of malignancy
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