

Nomenclature

Sarcomas	Mesenchymal tumors
Carcinomas	Epithelial tumors

Epidemiology (Acquired predisposing conditions)

1. Chronic inflammation
2. Immunodeficiency states
3. Precursor lesion

Clinical aspects

1. Local effects of tumor encroachment of tissues/ organs
- 2a. Functional activity e.g. Hormone synthesis
- 2b. Paraneoplastic syndromes -> Ectopic hormone secretion
3. Bleeding & infections when tumor ulcerates thru adjacent surface
4. Rupture/ infarction
5. Cachexia (Weakness, e.g. weight loss)

Molecular basis of cancer

Nonlethal genetic damage

Hallmark: Genetic alteration

Cancer genes (Target of genetic damage)

1. Oncogene (Mutated gene)

- Mutation from proto-oncogenes

2. Tumor suppressor genes

- Prevent uncontrolled growth

3. Apoptosis-regulating gene

- Overexpressed in cancer cell-> Protect against apoptosis

4. Regulate interactions between tumor and host cells

- Change recognition of tumor by host immune system

2. Insensitivity to Tumor suppressor signals

Retinoblastoma Gene

- Active hypophosphorylated state: Halts cell cycle
- Inactive hyperphosphorylated state
- Heterozygosity: X Affect cell function
- Both to be inactivated to affect function

p53

1. Cell cycle arrest
2. DNA repair

2. Insensitivity to Tumor suppressor signals (cont)

3. Apoptosis

4. Evasion of cell death

- Overexpression of BCL-2 protein -> Long life

8. Evasion of immune surveillance

Host defence against tumor -- Tumor immune

Tumor antigens

- Overexpressed cellular proteins, Oncogenic viral products, Differentiation antigens

- Oncogenic viral products

- Differentiation antigens

Antitumor effectors

- CD8+

- NK lymphocytes

- Macrophages

- Humoral immunity

Immune evasion

- Immunosuppression

- Antigen masking

- Apoptosis of CD8+

- Selective outgrowth

- X MHC expression

- X Costimulation

10. Tumor-promoting inflammation

- Interaction between inflammatory cell& tumor

1. Proliferation-promoting factor release

2. Growth suppressor removal

3. Cell death resistance

4. Angiogenesis

5. Invasion & Metastasis

6. Immune evasion

Benign Malignant differentiation

Benign	Malignant
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Differentiation & anaplasia

- | | |
|------------------------|--|
| 1. Well differentiated | 1. Well to undifferentiated (Anaplasia: Functional& structural differentiation loss) |
|------------------------|--|

- Dysplasia (Disordered growth)



Benign Malignant differentiation (cont)

- Carcinoma in situ (Non-invasive malignant tumor)

Rate of growth

- Correlates w./ level of differentiation

2. **Progressive & slow** 2. **Erratic** (Unpredictable)

Local invasion

3. **No**, expansion w./ clear boundaries 4. **Yes**, infiltrate & destroy

Metastasis

(1) Seeding of body cavities (2) Lymphatic spread (3) Hematogenous spread

4. **Absent** 4. **Frequently present**

1. Self-sufficiency in growth signals

Proto-oncogenes -Normal genes, promote proliferation

Oncogenes -Mutant version, function anonymously w./o growth-promoting signals

Oncoproteins -Proteins encoded

Self-sufficient in:

1. **Growth factors & receptors** 3. **Transcription factors**

2. **Signal transduction proteins** 4. **Cyclins & CDKs**

3. Altered cellular metabolism

Warburg effect

- Aerobic situation: Distinct form of cellular metabolism

- **High levels of glucose uptake**

- **Increased conversion of glucose to lactose via glycolytic pathway**

5. Limitless replicative potential: Telomerase

- Telomerase shorten with each cell division

- Cancer cell have enzyme that regenerate telomerase

6. Sustained angiogenesis

- Controlled by balance between angiogenesis promoter (VEGF) and inhibitors (bFGF)

7. Invasion & Metastasis

- Invasion of extracellular matrix

a. Loosening of intracellular junctions

b. Degradation

c. Attachment

d. Migration

- Embolus: Evade WBC killing

9. Genetic instability

- Both copies of DNA repair proteins are lost

1. Hereditary Nonpolyposis Cancer Syndrome

2. **BRCA-1 & BRCA-2** (80% familial breast cancer, not sporadic-associated)

Carcinogenic Agents

1. Chemical Carcinogenesis

Initiation

- Carcinogen exposure -> permanent DNA

Promotion

- Promoter induce tumor in initiated cell (Nontumorigenic)

- Promoting agent enhance proliferation & results in cancer

2. Radiation Carcinogenesis

- UV rays (UVB, 280-320nm)

- Ionizing radiation (X-ray, gamma ray, particles)

3. Oncogenic DNA viruses

1. Papillomaviruses (HPV)

2. Epstein-Barr virus (EBV)

3. Hep B virus (HBV)

4. Kaposi sacroma herpes virus (KSHV)

