

### Nomenclature

<b>Sarcomas</b>	Mesenchymal tumors
<b>Carcinomas</b>	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

#### Antitumor effectors

- |   |                    |
|---|--------------------|
| - Overexpressed cellular proteins, Oncogenic viral products, Differentiation antigens | - CD8+             |
| - Oncogenic viral products  | - NK lymphocytes   |
| - Differentiation antigens  | - Macrophages      |
|   | - Humoral immunity |

#### Immune evasion

- |                     |                       |
|---------------------|-----------------------|
| - Immunosuppression | - Selective outgrowth |
| - Antigen masking   | - X MHC expression    |
| - Apoptosis of CD8+ | - 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

#### Differentiation & anaplasia

- |                               |   |
|-------------------------------|---|
| 1. <b>Well differentiated</b> | 1. <b>Well to undifferentiated</b> (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**
- 2. Signal transduction proteins**
- 3. Transcription factors**
- 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 sarcoma herpes virus (KSHV)**

