Nomenclature

Sacromas	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	**Antitumor effectors**
- Overexpressed cellular proteins, Oncogenic viral products, Differentiation antigens	- CD8+
- Oncogenic viral products	- NK lymphocytes
- Differentiation antigens	- Macrop-hages
	- Humoral immunity
Immune evasion	
- Immunosuppression	- Selective outgrowth
- Antigen masking	- X MHC expression
- Apoptosis of CD8+	- X Costim-ulation

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. **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

Warbug effect

- Aerobic situation: Distinct form of cellular metabolism

- High levels of glucose uptake

- Increased conversion of glucose to lactose via glycoyitic 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. Attatchment

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)