Neoplasia

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General Considerations

Overview:

- **Neoplasia** – uncontrolled, disorderly proliferation of cells resulting in benign or malignant neoplasm
- **Dysplasia** – reversible change. Precedes malignant transformation
  - Disorderly maturation, spartial arrangement of cells, marked variability in nuclear size & shape (pleomorphism) increased abnormal mitosis.
- Neoplasms – well differentiated or poorly differentiated.

Classification & Nomenclature of Tumors

- Behavior – benign or malignant
- Described based on appearance
- Tissue of origin
- Degree of differentiation
  - Well differentiated
  - Poorly differentiated

Malignant Tumors

- **Invasive** – spread into adjacent structures
- **Metastasis** – implantation of tumor cells into distant sites. Most important defining feature.
- Less differentiated compared to benign tumors
- **Anaplasia** – poorly differentiated. Exhibit pleomorphism, hyperchromatism (dark staining nuclei) and increased nuclear-cytoplasmic ratio, abnormal mitosis, cellular dyspolarity and prominent nucleoli.
- *Paradoxically most aggressive tumors respond well to chemotherapy & radiotherapy*

Malignant Tumors

- Carcinoma – epithelial cell origin
- Adenocarcinoma – glandular epithelial cell origin
- Sarcoma – mesenchymal cell origin. Often used as a prefix to denote tissue of origin. E.g osteosarcoma.
- Eponymically named tumors – specific names. E.g. Burkitts lymphoma
- Teratoma – germ cell origin.

Benign Tumors

- Well differentiated
- Encapsulated
- Slow growing and do not metastasis
- Often denoted by the suffix –oma. E.g. lipoma.

Benign Tumors

- Papilloma – surface epithelial origin
- Adenoma – glandular epithelium
- Mesenchymal origins – named according to tissue of origin. E.g. fibroadenoma – fibrous tissue with glandular epithelium
- Hamartoma – non-neoplastic disorganised tumor like overgrowth of cell types within an affected organ. E.g. hemangioma – irregular accumulation of blood vessels

Properties of Neoplasms

- Monoclonality – denotes origin from a single precursor cell.
- Markers of monoclonality
  - Isoenzymes
  - Genes
  - Specific translocations
  - Immunoglobulins
  - Immunoglobin gene rearrangements
  - Cell surface markers

Clinical Features of malignancy

- Cachexia and wasting – TNF-α a product of macrophages that promotes catabolism of fatty tissue.
- Endocrine abnormalities – caused by tumours of endocrine gland origin
- Paraneoplastic syndroms – ectopic production & secretion of hormones or chemically unrelated substances inducing effects similar to those of a given hormone. E.g. MEN I, MEN II
- Oncofetal antigen – expression of embryonic Ag in adults. Manifestation of dedifferentiation.

Carcinogenesis & Etiology

- Endogenous & Exogenous factors recognised.
- Chemicals, physical agents, viruses, activation of cancer-promoting genes and inhibition of cancer-suppressing genes.
- Chemical carcinogens:
  - Direct-reacting – do not require chemical alteration to act
  - Indirect-reacting – require metabolic coversion from procarcinogens to active ultimate carcinogens

Stages of chemical carcinogenesis

- Initiation – 1st critical step. Reaction between carcinogen & DNA. 2 or more agents may act as cocarcinogens.
- Promotion – induced by stimulation of cell proliferation. A promoter, not carcinogenic in itself enhances other agents' carcinogenecity.

Radiation Carcinogensis

- Exposure to ultraviolet radiation – dimer formation between neighboring thymine pairs in DNA. Failure of repair results in skin cancers.
- Ionizing radiation – classic cause of cancer. Persons exposed to radiation have very increased risk of cancers.
- Viral carcinogens – DNA and Retroviruses.
  - DNA viruses – integrate viral DNA into host genomes.
  - Retrovises – substitution of viral oncogenes into host genomes

Oncogenes & Cancer

- **Protein products of proto-oncogenes play essential role in DNA replication and transcription**
- **Mechanisms of action of oncogenic protein products:**
  - **Activation by binding of GTP. E.g. Ras ongogenes that code for p21 proteins, similar to G proteins. Mediate signal transduction from cell surface.**
    - **Mutated ras gene – occurs at codon 12 resulting in abnormal p21 protein. Mutated ras proteins activated by GTP but cannot be inactivated by GTPase.**
    - **Result: sustained signal transduction leading to continued cell proliferation**

Oncogenes & Cancer

- Protein tyrosine kinase activity:
  - Abnormal tyrosine kinase can not be inactivated.
  - Result is sustained signal transduction
- Growth Factor or growth factor receptor activity
  - Inappropriate activation of receptor proteins mimicking growth factors.
- Nuclear proteins
- Protein products confined to nucleus

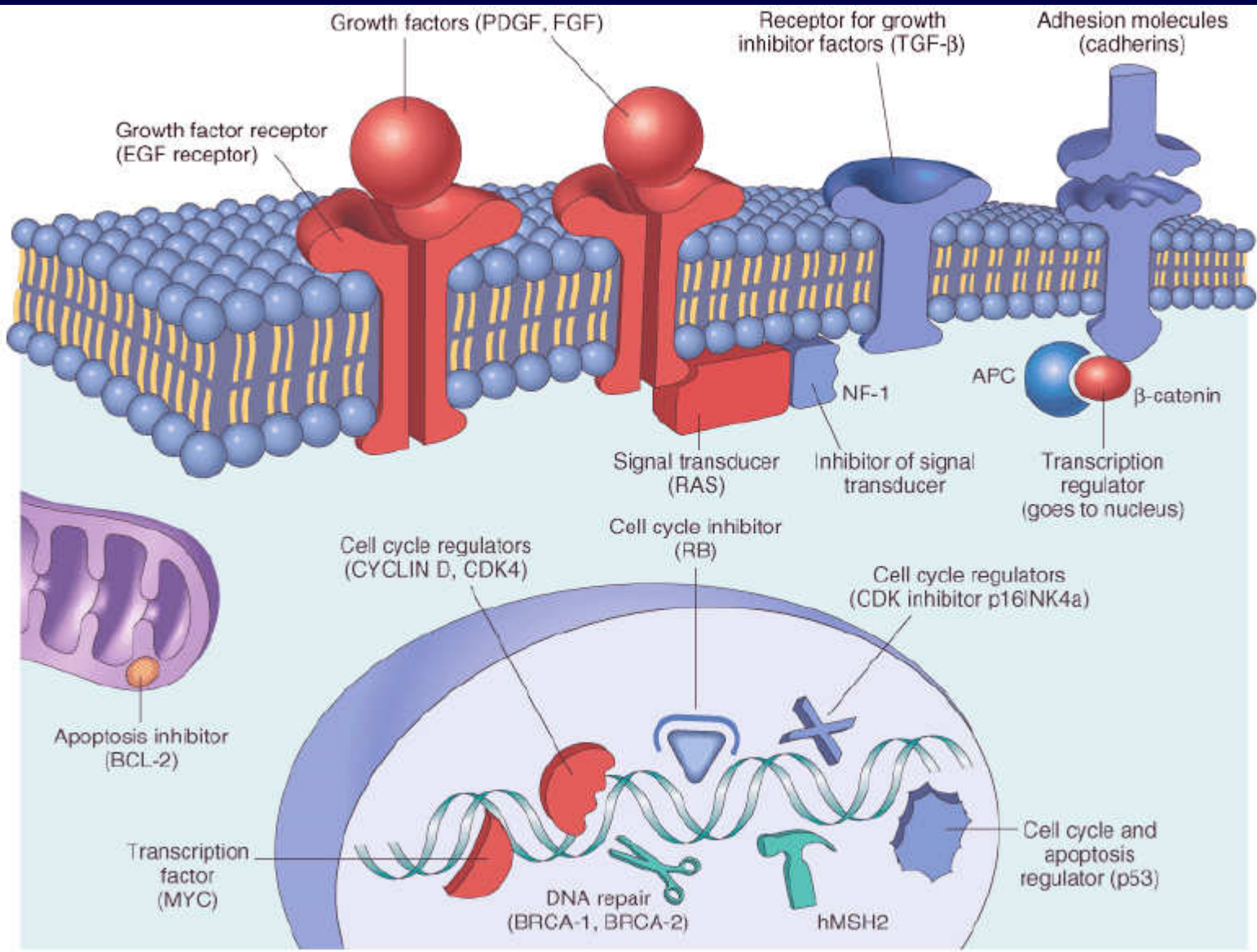

TABLE 7-8 -- Selected Oncogenes, Their Mode of Activation, and Associated Human Tumors

Ongogenes & Human Cancer

- Mechanisms by which c-cons become tumorigenic:
  - Promoter insertion (insertional mutagenesis): insertion of promoter or enhancer sequences into host genome
  - Point mutations: single nucelotide changes.
  - Chromosomal translocations: frequent at sites of chromosomal breaks
  - Gene amplification: reduplication of genes.

Tumor Suppressor Genes

- Normal: Cancer suppressor genes promote cell proliferation when gene is ACTIVATED.
- Inactivation of tumor suppressor genes leads to cancer.

Grading & Staging

- Required for prognosis & clinical management
- Grading: histopathological evaluation based on degree of cellular differentiation
- Staging: degree of localization or spread of tumor.
- TNM classification – tumor size, lymp node involvement and metastasis
- Specific classification for specific tumors. E.g. Duke system for colorectal carcinoma.

End

- Robins Pathological Basis of Diseases – what ever edition you have.

- PDF format of presentation & study guides will be available on:

www.pathologyatsmhs.wordpress.com