GENERAL ONCOLOGY
Tumours ....omas

• Tumour = abnormal tissue swelling (hyperplasia, inflammation, cysts....)

• Tumour = neoplasia = autonomous abnormal cell growth, which persists after the initiating stimulus has been removed.
STRUCTURE OF TUMOURS

1) **tumour parenchyma** = neoplastic cells (**homologic t.** versus **heterologic t.**)

Anaplastic t. resemble to embryonal organs

2) **tumour** stroma - mechanical support and nutrition

(organoid versus histoid t.)

- **Organoid** t. stroma well differentiated from parenchyma (carcinomas)
- **Histoid** - nearly impossible to distinguish stroma from parenchyma (mesenchymal tu)

- **Medullary tu** – predominance of parenchyma, soft consistency
- **Scirhotic tu** - predominance of stroma, hard consistency

Connective tissue (desmoplastic stroma)

Neoangiogenesis (VEGFx angiostatin, endostatin),

Independence on angiogenesis - up to 1-2 mm
CLASSIFICATION OF TUMOURS

1) Behaviour:
   - benign
   - malignant
   - potentially malignant (PA)
   - semimalignant (bazalioma – destruction but no metastases)

2) Histogenesis: – origin of cells
   (epithelial, mesenchymal, neuroectodermal, germ-cell tumours and teratomas, mesothelial, trophoblastic, mixed tumours)
<table>
<thead>
<tr>
<th>Feature</th>
<th>Benign</th>
<th>Malignant</th>
</tr>
</thead>
<tbody>
<tr>
<td>Growth rate</td>
<td>Slow</td>
<td>Relatively rapid</td>
</tr>
<tr>
<td>Mitotic activity</td>
<td>Low</td>
<td>High</td>
</tr>
<tr>
<td>Histological resemblance to normal tissue</td>
<td>Good</td>
<td>Variable, often poor</td>
</tr>
<tr>
<td>Nuclear morphology</td>
<td>Often normal</td>
<td>Usually hyperchromatic, irregular outline, multiple nucleoli and pleomorphic</td>
</tr>
<tr>
<td>Invasion</td>
<td>No</td>
<td>Yes</td>
</tr>
<tr>
<td>Metastases</td>
<td>Never</td>
<td>Frequent</td>
</tr>
<tr>
<td>Border</td>
<td>Often circumscribed or encapsulated</td>
<td>Often poorly defined or irregular</td>
</tr>
<tr>
<td>Necrosis</td>
<td>Rare</td>
<td>Common</td>
</tr>
<tr>
<td>Ulceration</td>
<td>Rare</td>
<td>Common on skin or mucosal surfaces</td>
</tr>
<tr>
<td>Direction of growth on skin or mucosal surfaces</td>
<td>Often exophytic</td>
<td>Often endophytic</td>
</tr>
</tbody>
</table>
A Benign
- Intact surface
- Exophytic growth
- Homogeneous cut surface
- Circumscribed or encapsulated edge

B Malignant
- Heterogeneous cut surface due to necrosis
- Ulcerated surface
- Endophytic growth
- Vascular permeation
- Irregular infiltrative edge
FEATURES OF MALIGNANT CELLS

- Immortality- (normal cells – 50 mitotic cycles x transformed – without a limit)
- Independence on adjacent metabolic conditions (self autocrine and paracrine stimulation)
- Ability to growth at anaerobic conditions
- Lack of contact inhibition (increase od saturation density)
- Atypias
- Aggressive and infiltrative growth = invasive growth
  Increased adhesion to basement membrane (laminin, fibronectin, → disruption of basal membrane → migration
- Metastases
1) tissue a. (loss of regular arrangement, loss of polarization and stratification, desmoplastic stroma)

2) cellular

   a) cytoplasmic (↑ size, changes of specialized structures-cillias, irregular shape, cannibalisms, increased basofilia - ↑RNA, structural rearrangement (cytoskeleton)
b) nuclear a. - ↑nuclear size (N/C ratio
normal cells N/C=1:4, 1:6
malignant 1:1 anh higher)
- hyperchromasia (↑DNA, tetraploid, polyploid, aneuploid)
  - increase and enlargement of nucleoli
  - rearrangement of chromatin
c) mitoses - ↑number, atypical
Fig. 1 – Malignant cell characteristics.
METASTASES

discontinuous propagation

(less than 0.1% released cells)

Micrometastases (0.2-2mm, only 1% will progress)

Macrometastases

1. phase = release

2. phase Transport to a new place

3. phase - Nidation (tromboxan, CD44)
MECHANISMS OF TUMOR INVASION AND METASTASIS

• Interstitial collagenases - degradation collagen I, II, III
• Gelatinases - collagen IV - gelatin
• Stromelysins - collagen IV and stromelysis
METASTATIC CASCADE

- **Detachment**
  - Loss of surface adhesion molecules (e.g., cadherins)
  - Consequences: Migration of individual cells enabled

- **Invasion**
  - Metalloproteinases
  - Up regulation of integrin expression
  - Down regulation of tissue inhibitors of metalloproteinases
  - Consequences: Erosion of tissue boundaries

- **Intravasation**
  - Metalloproteinases
  - Down regulation of tissue inhibitors of metalloproteinases
  - Consequences: Access to vascular routes of dissemination

- **Evasion of host defences**
  - Reduced expression of MHC class 1 antigen
  - Shedding of ICAM-1 blocks T-cell receptor
  - Consequences: Survival against host defences

- **Arrest**
  - Binding of CD44 to endothelial ligand
  - Consequences: Arrest of movement by adhesion to endothelium

- **Extravasation**
  - Integrins
  - Laminin receptor
  - Consequences: Colonisation of site of metastasis
TYPE OF METASTASES

a) Porogenic =transcoelolomic and implantant
b) Lymphogenic (carcinomas)
c) Haematogenic (v. cava, v.portae, arterial) (sarcomas)

-selective metastases (prostatic ca → vertebras) X systemic m.
-histohomologic metastases x systemic metastazes (IGF, antiproteases…)
- solitary m. X multiple
- late m. X early m.
TUMOROUS MULTIPLICITY

- 1) secondary multiplicity = metastases
- 2) primary multiplicity

A) Simultaneous (at the same time)
   aa) systemic (BRCA1,2 – ovarial and breast ca)
      bb) local (in one organ – multiple bazaliomas)

B) Successive (consequently)
CLINICAL EFFECT OF TU

1) local
   – compression, invasion, ulceration, adjacent tissue destruction
Pituitary adenoma – atrophy of the gland – hypopituitarism
- Bleeding – massive x chronic- anemia
  - thrombosis
- Intracranial pressure
- Obstruction (eosophagus, ureters, lymph drainage)
<table>
<thead>
<tr>
<th>Local effect</th>
<th>Result</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mass</td>
<td>Presentation as tissue lump or tumour</td>
</tr>
<tr>
<td>Ulcer (non-healing)</td>
<td>Destruction of epithelial surfaces (e.g., stomach, colon, mouth, bronchus)</td>
</tr>
<tr>
<td>Haemorrhage</td>
<td>From ulcerated area or eroded vessel</td>
</tr>
<tr>
<td>Pain</td>
<td>Any site with sensory nerve endings; tumours in brain and many viscera are initially painless</td>
</tr>
<tr>
<td>Seizures</td>
<td>Tumour mass in brain; seizure pattern often localizes the tumour</td>
</tr>
<tr>
<td>Cerebral dysfunction</td>
<td>Wide variety of deficits depending on site of tumour</td>
</tr>
<tr>
<td>Obstruction</td>
<td>Of hollow viscera by tumour in the wall</td>
</tr>
<tr>
<td>Perforation</td>
<td>Of viscera</td>
</tr>
<tr>
<td>Bone destruction</td>
<td>Pathological fracture, collapse of bone</td>
</tr>
<tr>
<td>Inflammation</td>
<td>Of serosal surface</td>
</tr>
<tr>
<td>Effusions</td>
<td>Pleural effusion, pericardial effusion, ascites</td>
</tr>
<tr>
<td>Space-occupying lesion</td>
<td>Raised intracranial pressure in brain neoplasms; anaemia due to displacement of haematopoietic cells by metastases to the bone marrow</td>
</tr>
<tr>
<td>Loss of sensory or motor function</td>
<td>Compression or destruction of nerve or nerve trunk</td>
</tr>
<tr>
<td>Oedema</td>
<td>Due to venous or lymphatic obstruction</td>
</tr>
</tbody>
</table>
CLINICAL EFFECT

2) metabolic

a) Tumour type specific
   - thyreotoxicosis, Cushing’s sy, hyperparathyroidism

b) Non specific
   aa) hyperuricaemia
   - hypoglycaemia
   - amyloidosis
   - RTLS – rapid tumour lysis sy (Hyperuricaemis, fosfataemia, hypocalcaemia, hyperkalaemia → arrhytmias
   bb) Cachexia-loss of fatty tissue and muscles

- Toxic products – cachectins = TNF alpha, IL-1, INF gamma
  cc) Paraneoplastic sy (neuropathies, myopathies (lung, breast), anemia = autoimmune, polycytemia (erythropoetin), migrating thromboises = Trousseau´s sy, immunosupression
DEATH REASONS

• 1) escalated complication (mechanical, chemical, metabolical, endocrine, cachexia, immunosupression

• 2) after therapy (opportunistic i., toxic effect, b. marrow atrophy)
PROGNOSIS

1) Tumour type = typing (good – bazalioma, seminoma
intermediate – breast, colon, kidney ca
poor- ca lung, pancreas, stomach, liver

2) Tumour grade = grading - degree of differentiation+mitotic
activity+cellular and nuclear pleomorfism
Well, moderately, poorly, undifferentiated
Low grade x high grade (intermediate grade)

3) Tumour stage = staging - extend of the spread
Duke´s classification (colorectal ca)
Clark´s and Breslow classification (melanoma)
TNM classification !!!!!!!!!!!!!!
TNM SYSTEM FOR STAGING OF TUMOURS

T
(Tumour size)

N
(Degree of lymph node involvement)

M
(Extent of distant metastases)

Example: Primary tumour
Lymph nodes
Distant metastases (none)

= T2 N1 M0

Prognosis
Molecular biological markers:
• Mutation analysis (GIST)
• EGFR (colon, lung)
• Her2/neu (breast)
HOST FACTORS IN CARCINOGENESIS

- Race
- Diet (carcinegenes, lack of protective factors, obesity)
- Inherited risks
- Age (kids x adults)
CARCINOGENS

• **carcinogens** is any substance, that is an agent directly involved in causing cancer
• Co-carcinogens are chemicals that do not necessarily cause cancer on their own, but promote the activity of other carcinogens in causing cancer

• 1) **chemicals** Tar, asphalt, dyes, smoked meat,
• Metals – azbest, arsenic, nickel, cobalt

• 2) **physical** (radiation gamma, UV)
  mechanical irritation, shape – implants, heat)
• 3) **biological** – viruses,
  Moulds – aflatoxins
  bacterias, parasites
  (H. pylori, bilharsiosis)
Fig. 4 – New proposal to classify chemical carcinogens.
### Table II: Chemical carcinogens.

<table>
<thead>
<tr>
<th>Group</th>
<th>Compound</th>
<th>Mechanism of action</th>
<th>Affected organs/Cancer type</th>
</tr>
</thead>
<tbody>
<tr>
<td>Polycyclic aromatic hydrocarbons</td>
<td>Benzo[a]pyrene, Polychlorinated biphenyls (Luch 2005)</td>
<td>Form adducts with purine bases of DNA, mainly resulting on transversions</td>
<td>Skin, lungs, stomach, Liver, skin</td>
</tr>
<tr>
<td>Aromatic amines/amides</td>
<td>2-Acetylaminofluorene, 4-Aminobiphenyl, 2-Naphthylamine (Luch 2005)</td>
<td>Genotoxic compounds, increase the rate of cell duplication</td>
<td>Liver, bladder, Bladder, Bladder</td>
</tr>
<tr>
<td>Aminoazo dyes</td>
<td>o-Aminoazoazolone, N, N-dimethyl-4-aminoazobenzene (Golka et al. 2004)</td>
<td>Forms adducts with DNA and with haemoglobin</td>
<td>Liver, lungs, bladder, Lungs, liver</td>
</tr>
<tr>
<td>N-nitroso compounds</td>
<td>N-Nitrosodimethylamine (Drablos et al. 1998)</td>
<td>Form adducts at N- and O-atoms in DNA bases</td>
<td>Liver, lungs, kidneys</td>
</tr>
<tr>
<td>Carbamates</td>
<td>N-methylcarbamate esters (Wang et al. 1998)</td>
<td>Chromosome aberration, gene mutation, cell transformation</td>
<td>Experimental results showed liver, kidneys and tests degeneration</td>
</tr>
<tr>
<td>Halogenated compounds</td>
<td>Trichloroethylene (Lock et al. 2007)</td>
<td>Somatic mutations, modification of cell cycle pathways</td>
<td>Experimental results showed kidney, liver and lung cancer</td>
</tr>
<tr>
<td>Natural carcinogens</td>
<td>Aflatoxin B1 (Wild et al. 1986), Asbestos (Luch 2005)</td>
<td>Forms adducts with guanine, react with RNA and proteins</td>
<td>Liver, Lungs</td>
</tr>
<tr>
<td>Metals</td>
<td>Arsenic (Shi et al. 2004), Cadmium (Hartwig et al. 2002), Nickel (Costa et al. 2003)</td>
<td>Oxidative stress, Inhibit DNA repair pathways and nucleotide-excision repair, Histone acetylation and DNA hypermethylation</td>
<td>Skin, lungs, liver, Lungs, prostate, kidneys, Lungs, nasal cavity</td>
</tr>
<tr>
<td>Anticancer drugs</td>
<td>Alkylating agents (Luch 2005)</td>
<td>Interstrand and/or intrastrand cross-links</td>
<td>Leukaemia</td>
</tr>
</tbody>
</table>
ONCOGENIC VIRUSES

1) DNA
   a) HPV 16,18,31,33,51 (Cervical, laryngeal, anal ca)
   b) Herpetic viruses- EBV (Burkitt’s lymphoma, HD, nasopharyngeal ca
      - KSHV8 (Kaposi’s sarcoma, pleural effusion lymphoma
   c) HBV

2) RNA – strongly oncogenic (oncogenes)= direct transformation
   - weakly oncogenic (activation of natural cellular oncogenes)

   Flaviviridae- HCV
   Retroviadae HTVL-1 (T leucaemia)

   animals (Abelson leucaemia-v-abl, Rous sarcoma- v –src,
      avian myelocytomatosis – c-myc, avian myeloblastomatosis – v-myb,
      avian erythroblastosis – v-erb,
      Harvey’s sarcoma v-H-ras, Kirsten’s sarcoma v-K-ras, simian sarcoma v-sis)
   Humans- HTVL-1
MECHANISMS OF INTEGRATION OF ONCOGENIC VIRAL GENES, OR DNA TRANSCRIPTS, INTO THE HOST CELL DNA

(A) Oncogenic DNA virus

1. Infection
2. Host cell
3. Integration
4. Transformation
5. Neoplastic cell
6. Integrated viral gene

(B) 'Acute' transforming oncogenic RNA virus

1. Infection
2. Host cell
3. Virus
4. Cellular oncogene
5. RNA transcript
6. Virus with cellular oncogene incorporated in its genome
7. Transduction into host cell
8. Neoplastic cell
9. Integrated DNA transcript of oncogene RNA

(C) 'Slow' transforming oncogenic RNA virus

1. Infection
2. Host cell
3. Virus
4. Promoter gene
5. DNA transcripts of viral promoter gene
6. Cellular oncogene
7. DNA transcripts of viral promoter gene inserted next to oncogene which is thus activated
8. Neoplastic cell
9. Neoplastic cell
• Standard morphological tissue alterations associated with a cancer significantly more frequently, when compared to healthy tissue of the same histogenetic origin or localization.

Classification

1) Non progredient = stational (epithelial hyperplasia, testicular retention, burns, metaplasia – squamous, glandular, intestinal)

2) Progredient (hyperproliferation, cellular atypia= atypical epithelium
dysplasia= intraepithelial neoplasia (CIN, VIN, VAIN, GIN, PIN)

a-) Mild

B) Moderate

c) High grade /CIS (Carcinoma in situ)
<table>
<thead>
<tr>
<th>Precancerous lesion</th>
<th>Cancer</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Hyperplasia</strong></td>
<td>Endometrial carcinoma</td>
</tr>
<tr>
<td>Endometrial hyperplasia</td>
<td>Breast carcinoma</td>
</tr>
<tr>
<td>Breast-lobular and ductal hyperplasia</td>
<td>Hepatocellular carcinoma</td>
</tr>
<tr>
<td>Liver—cirrhosis of the liver</td>
<td></td>
</tr>
<tr>
<td><strong>Dysplasia</strong></td>
<td></td>
</tr>
<tr>
<td>Cervix</td>
<td>Squamous carcinoma</td>
</tr>
<tr>
<td>Skin</td>
<td>Squamous carcinoma</td>
</tr>
<tr>
<td>Bladder</td>
<td>Transitional carcinoma</td>
</tr>
<tr>
<td>Bronchial epithelium</td>
<td>Lung carcinoma</td>
</tr>
<tr>
<td><strong>Metaplasia</strong></td>
<td></td>
</tr>
<tr>
<td>Glandular metaplasia of oesophagus</td>
<td>Adenocarcinoma of the oesophagus</td>
</tr>
<tr>
<td>Intestinal metaplasia of the stomach</td>
<td>Adenocarcinoma of the stomach</td>
</tr>
<tr>
<td>Squamous metaplasia of the bronchus</td>
<td>Lung carcinoma</td>
</tr>
<tr>
<td><strong>Inflammatory lesions</strong></td>
<td></td>
</tr>
<tr>
<td>Ulcerative colitis</td>
<td>Adenocarcinoma of the colon</td>
</tr>
<tr>
<td>Atrophic gastritis</td>
<td>Adenocarcinoma/lymphoma of the stomach</td>
</tr>
<tr>
<td>Autoimmune (Hashimoto’s thyroiditis)</td>
<td>Malignant lymphoma/thyroid carcinoma</td>
</tr>
<tr>
<td><strong>Benign neoplasms</strong></td>
<td></td>
</tr>
<tr>
<td>Neurofibroma</td>
<td>Malignant schwannoma</td>
</tr>
<tr>
<td>Colonic adenoma</td>
<td>(malignant peripheral nerve sheath tumour)</td>
</tr>
<tr>
<td></td>
<td>Adenocarcinoma of the colon</td>
</tr>
</tbody>
</table>
**Table 11.13  Diseases associated with an increased risk of neoplasia.**

<table>
<thead>
<tr>
<th>Non-neoplastic disease</th>
<th>Neoplasm</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mongolism (trisomy 21)</td>
<td>Acute myeloid leukaemia</td>
</tr>
<tr>
<td>Xeroderma pigmentosum (plus sun exposure)</td>
<td>Squamous cancer of skin</td>
</tr>
<tr>
<td>Gastric atrophy (pernicious anaemia)</td>
<td>Gastric cancer</td>
</tr>
<tr>
<td>Tuberous sclerosis</td>
<td>Cerebral gliomas</td>
</tr>
<tr>
<td>Café au lait skin patches</td>
<td>Neurofibromatosis (dominant inheritance); acoustic neuroma,</td>
</tr>
<tr>
<td></td>
<td>phaeochromocytoma</td>
</tr>
<tr>
<td>Actinic dermatitis</td>
<td>Squamous carcinoma of skin;</td>
</tr>
<tr>
<td></td>
<td>malignant melanoma</td>
</tr>
<tr>
<td>Glandular metaplasia of oesophagus (Barrett’s oesophagus)</td>
<td>Adenocarcinoma of oesophagus</td>
</tr>
<tr>
<td>Dysphagia and anaemia (Plummer–Vinson syndrome)</td>
<td>Oesophageal cancer</td>
</tr>
<tr>
<td>Cirrhosis (alcoholic, hepatitis B)</td>
<td>Hepatocellular carcinoma</td>
</tr>
<tr>
<td>Ulcerative colitis</td>
<td>Colonic cancer</td>
</tr>
<tr>
<td>Paget’s disease of bone</td>
<td>Osteosarcoma</td>
</tr>
<tr>
<td>Immunodeficiency states</td>
<td>Lymphomas</td>
</tr>
<tr>
<td>AIDS</td>
<td>Lymphoma, Kaposi’s sarcoma</td>
</tr>
<tr>
<td>Autoimmune disease (e.g. Hashimoto’s thyroiditis)</td>
<td>Lymphoma (e.g. thyroid lymphoma)</td>
</tr>
<tr>
<td>Dysplasias (e.g. cervical dysplasia)</td>
<td>Cancer</td>
</tr>
</tbody>
</table>

AIDS, Acquired immune deficiency syndrome.
PATHOGENESIS OF TUMOUR GROWTH

1. **Phase of induction** (15-30yrs)
   a) Initiation (irreversible changes of cell genotype – mutations, → normal phenotype
   initiators – cancerogens
   b) Latency – cummulation of changes → atypical cells
   c) Promotion (in latin = promoce) → clonal selection (promoters- co-carcinogens

2. **Blastoma in situ** = expansion of a malignant clone

3. **Progression** – invasion+dissemination
REGULATION OF THE CELL CYCLE

- DNA damage
- Oncogenic activation
- Hypoxia

Growth Factors and Cytokines

Proloconcogenes

p53

CDK inhibitors

Cyclins D, E
CDK 2, 4, 6

Rb
E2F

Rb
P
E2F

Go

G1

R

APOPTOSIS

M
G2

Cyclins A and B
CDK's
GENETIC MECHANISMS OF CARCINOGENESIS

• expression of telomerase (avoid senescence from telomeric shortening)
• inactivation of tumour suppressor genes
• activation of oncogenes
### TUMOUR SUPPRESSORS

<table>
<thead>
<tr>
<th>Gatekeepers</th>
<th>p53</th>
<th>50% human cancers</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rb1</td>
<td></td>
<td>human cancers</td>
</tr>
<tr>
<td>APC (beta catenin)</td>
<td></td>
<td>Colorectal ca</td>
</tr>
<tr>
<td>Carekakers</td>
<td></td>
<td></td>
</tr>
<tr>
<td>BRCA1</td>
<td></td>
<td>Breast, ovarian</td>
</tr>
<tr>
<td>BRCA2</td>
<td></td>
<td></td>
</tr>
<tr>
<td>MSH1, MSH2</td>
<td></td>
<td>Hereditary non polyposis colorectal ca</td>
</tr>
</tbody>
</table>

- Other suppressors – WT1, WT2, (nephroblastoma)
  - NF1, 2
  (neurofibromas, schwannomas, gliomas)
  - VHL (renal ca, hemangiomas)
  - p16 (melanomas, eosophageal ca)
P53 Regulation of Genomic Integrity

Genotoxic Stress

- ARF
- MDM2
- p53

- Ubiquitin
- p53 Degradation

- GADD45
- DNA Repair

- CKI p21^{CIP1}

- Bax
- Apoptosis

- Cell cycle arrest

- Cyclins
- pRb
- E2f

- pRb
- E2f
- Cell cycle progression
LOSS OF TUMOUR INHIBITORY GENES (ANTI-Oncogenes)

Inherited absence of one of the paired Rb1 genes

Mutational loss of Rb1 gene in any retinal cell

Mutational loss of the other Rb1 gene in same cell or its daughter cells

High risk of bilateral retinoblastoma

Unilateral retinoblastoma

Inherited retinoblastoma

Sporadic retinoblastoma

Carcinogenic stimulus

Normal p53

Defective p53

Apoptotic cell death

Mutation repaired

Tumour
ONCOGENES

An oncogene is a gene that has the potential to cause cancer. In tumor cells, they are often mutated or expressed at high levels.

A proto-oncogene is a normal gene that can become an oncogene due to mutations or increased expression. The resultant protein may be termed an oncoprotein. Proto-oncogenes code for proteins that help to regulate cell growth and differentiation. Proto-oncogenes are often involved in signal transduction and execution of mitogenic signals, usually through their protein products. Upon activation, a proto-oncogene (or its product) becomes a tumor-inducing agent, an oncogene.
ONCOGENES

- Abl - protein-tyrosine kinase activity
- Myc – binds to DNA, directly stimulating synthesis (A)
- erbB (receptor for EGFR) (B)
- Sis (PDGF) (C)
- Ras – intracellular signalling (D)
<table>
<thead>
<tr>
<th>Inherited disorder</th>
<th>Tumour(s)</th>
<th>Comment</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Multiple endocrine neoplasia (MEN) syndromes</strong></td>
<td>Endocrine tumours, e.g. phaeochromocytoma, medullary carcinoma of the thyroid, parathyroid adenoma</td>
<td>Several types (MEN I, II, etc.) attributed to RET gene on chromosome 10 and others on chromosome 11</td>
</tr>
<tr>
<td><strong>Xeroderma pigmentosum</strong></td>
<td>Skin cancers, e.g. basal cell carcinoma, melanoma</td>
<td>Deficiency of DNA repair enzymes</td>
</tr>
<tr>
<td><strong>Familial polyposis coli</strong></td>
<td>Colorectal carcinoma</td>
<td>Preceded by numerous adenomatous polyps; autosomal dominant APC gene on chromosome 5</td>
</tr>
<tr>
<td><strong>von Hippel–Lindau syndrome</strong></td>
<td>Cerebellar haemangioblastoma, phaeochromocytoma, hypernephroma</td>
<td></td>
</tr>
<tr>
<td><strong>Li–Fraumeni syndrome</strong></td>
<td>Breast carcinoma, soft-tissue sarcomas</td>
<td>Autosomal dominant inheritance associated with abnormalities on chromosomes 13 (Rb1 gene), 11 and 17 (p53 gene)</td>
</tr>
<tr>
<td><strong>Retinoblastoma</strong></td>
<td>Retinoblastoma (frequently bilateral)</td>
<td>Inherited allelic loss of one inhibitory Rb1 gene on chromosome 13</td>
</tr>
<tr>
<td><strong>Familial breast carcinoma</strong></td>
<td>Breast carcinoma, Ovarian carcinoma (Prostatic carcinoma in male family members)</td>
<td>Attributed to mutated BRCA1 gene on chromosome 17</td>
</tr>
</tbody>
</table>