Genetics basis in carcinogenesis: L1

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Neoplasm #1: Learning objectives

- What causes cancer?
- What is the link between genes and cancer?
- How is cancer diagnosed?
- Can cancer be prevented?
Tumor vs Neoplasia

- **Tumor** (Latin for *swelling*)
- originally meant all forms of swelling

The Five Cardinal Signs of Inflammation

- **Calor** – Heat
- **Rubor** – Redness
- **Tumor** – Swelling
- **Dolor** – Pain
- **Functio lose** – Loss of function

**Tumor**: An abnormal growth of tissue.

*Tumor* is now considered synonymous with *neoplasm* (Gr., new growth).

Gouty arthritis
• Hypertrophy - increase in cell size
• Hyperplasia – increase in number of cells
• Metaplasia – cell type conversion

• Neoplasia – abnormal proliferation
• Dysplasia – maturation abnormality
• Anaplasia – dedifferentiation

• Desmoplasia – connective tissue growth
• Hypertrophy results from an increase in cell size, while hyperplasia is from an increase in cell number.
• **Hyperplasia** results from an increase in **cell number**.

**Acne**: sebaceous gland hyperplasia
**Metaplasia** (Greek: "change in form") is the reversible replacement of one differentiated cell type with another mature differentiated cell type.

<table>
<thead>
<tr>
<th>Tissue</th>
<th>Normal</th>
<th>Metaplasia</th>
<th>Stimulus</th>
</tr>
</thead>
<tbody>
<tr>
<td>Airways</td>
<td>Pseudostratified columnar epithelium</td>
<td>Squamous epithelium</td>
<td>Cigarette smoke</td>
</tr>
<tr>
<td>Urinary bladder</td>
<td>Transitional epithelium</td>
<td>Squamous epithelium</td>
<td>Bladder stone</td>
</tr>
<tr>
<td>Esophagus</td>
<td>Squamous epithelium</td>
<td>Columnar epithelium</td>
<td>Gastro-esophageal reflux (Barrett's Esophagus)</td>
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<tr>
<td>Cervix</td>
<td>Glandular epithelium</td>
<td>Squamous epithelium</td>
<td>Low pH of vagina</td>
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**Gastro-esophageal reflux**
Hyperplasia is associated with tumorigenesis.
• **Neoplasia** (Gr., *new growth*) is *the abnormal proliferation of cells.*
  - The growth of the cells exceeds, and uncoordinated with that of the normal tissues.
  - The growth persists in the same excessive manner even after cessation of the stimuli.
• **Neoplasms** may be
  • benign,
  • pre-malignant or
  • malignant.
• Different growth patterns in *benign* and *malignant* tumors
• **Dysplasia** (Gr. “abnormal growth”), is referred to abnormality of cellular development.

• Dysplasia, in which cell maturation and differentiation are delayed, can be contrasted with **metaplasia**, in which cells of one mature, differentiated type are replaced by cells of another mature, differentiated type.

• Dysplasia is often indicative of an **early neoplastic process**.
• Hyperplasia is associated with tumorigenesis.
**Dysplasia** is a term refer to an abnormality of maturation. It is typically used when the cellular abnormality is restricted to the originating tissue.

- Dysplasia is often indicative of an early neoplastic process.
- Dysplasia, in which cell maturation and differentiation are delayed.

![Dysplastic mucosa of colonic adenomas](image)

**Adenocarcinoma in situ**
- Anaplastic cells (cancer cells) display marked pleomorphism.

- Anaplastic nuclei are variable and bizarre in size and shape.

- The nuclei are characteristically extremely hyperchromatic.

- The nuclear-cytoplasmic ratio may approach 1:1.

- More important, mitoses are often.

- They may grow with total loss of communal structures, such as gland formation or stratified squamous architecture.
Anaplasia is the most extreme disturbance in cell growth encountered in the spectrum of cellular proliferations.

The malignant cells are arranged in trabecular and solid patterns, with gland formation.

Single strands of malignant cells

The malignant cells are arranged in trabecular and solid patterns, with gland formation.
• Malignant neoplasms are called cancers. They included:
  • Carcinoma *in situ* (*cancer at the site*). They do not invade and destroy basement membrane but, given enough time, will transform into invasive cancer.
• **Invasive cancers**;
  they invade and destroy the surrounding tissue, may form *metastases* and eventually kill the host.
Cancer cells can **invade and destroy healthy tissues**, and they **can spread** (metastasis) through the bloodstream and the lymphatic system to other parts of the body.

**Metastasis**

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Primary and secondary cancers. Artwork showing the spread of cancer from a primary site in the skin (upper left), through the bloodstream (centre), to form secondary cancers elsewhere in the body (right). The secondary locations shown here are the lungs, liver and a skeletal long bone. The body will produce white blood cells (orange spheres) to attack the cancer cells (purple), but once the cancer has spread (a process called metastasis), the prognosis is poor. Secondary and primary cancers can be treated by surgery and/or radiotherapy and chemotherapy, depending on the location of the tumours.
Laboratory demonstration
• Tumors arising from any germ layer or more than ones.
Malignant tumor of surface epithelium is called ‘carcinoma’.

- Lung: Bronchogenic carcinoma
- Skin, Squamous cell carcinoma
- Brain: Carcinoma

Endoderm

Ectoderm

Ectoderm
Malignant tumor of connective tissue is called ‘sarcoma’.

Malignant tumor of surface epithelium is called ‘carcinoma’.
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• ADENO -CARCINOMA
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• SARCOMA of MUSCLE / Rhabdomyo-sarcoma
Malignant tumor of connective tissue is called ‘sarcoma’.

SARCOMA of MUSCLE / Rhabdo-myxo-sarcoma
• Malignant tumor of connective tissue is called ‘sarcoma’. 
Cancer: A general name for more than 200 diseases in which abnormal cells grow out of control.

Cancer cells can invade and destroy healthy tissues, and they can spread (metastasis) through the bloodstream and the lymphatic system to other parts of the body.
• Most carcinoma METASTASIS via lymphatic and later on vascular routes.
• METASTASIS intra-abdominal tumor: LN / Liver
Sarcoma metastasis: using vascular as a major route.
The most common METASTASIS sites: Lungs / Liver
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TNM Staging: System of cancer: A system to describe the amount and spread of cancer in a patient's body.

T describes the size of the tumor and any spread of cancer into nearby tissue;

N describes spread of cancer to nearby lymph nodes; and

M describes metastasis (spread of cancer to other parts of the body).
Common presentation of tumor: a painless mass

- Ectoderm

Neoplasms / Tumor
Distinct tumor border with pseudo-capsule in a benign breast tumor: *Fibroaden-oma*
Different growth patterns in *benign* and *malignant* tumors

**Benign Growth**
- Normal tissue cells
- Connective tissue capsule
- Abnormal cells

**Malignant Tumor**
- Normal tissue cells
- Cancer cells
• Tumor composes of mamary ducts and fibrous tissue proliferation.
• Benign tumor of meninges: *Meningi-oma*

• Ectoderm
Pancreatic endocrine tumor: *Insulin-oma*
• Benign tumors, named ending up with – OMA, with exception these tumors are malignant:

• Hepatoma – primary tumor of liver parenchyma
• Lymphoma - primary tumor of lymph node
• Melanoma - tumor of melanocyte
• Seminoma - tumor arising from seminiferous tubule

• However in tumors, with their names ending up with – BLASTOMA, they are embryonal cell tumors, and all are malignant tumors, e.g.
• Neuro-blastoma,
• Retino-blastoma and
• Medalo-blastoma.
• Tumors arising from **any germ layer** or more than ones.
Is it tumor or what!?

Is it benign or malignant?
Teratoma: tumor originates from more than one germ-layers.

- 80-90%, benign teratoma
- 20-10%, malignant teratoma