



# **Cellular basis of cancer**

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**SpR Histopathology**

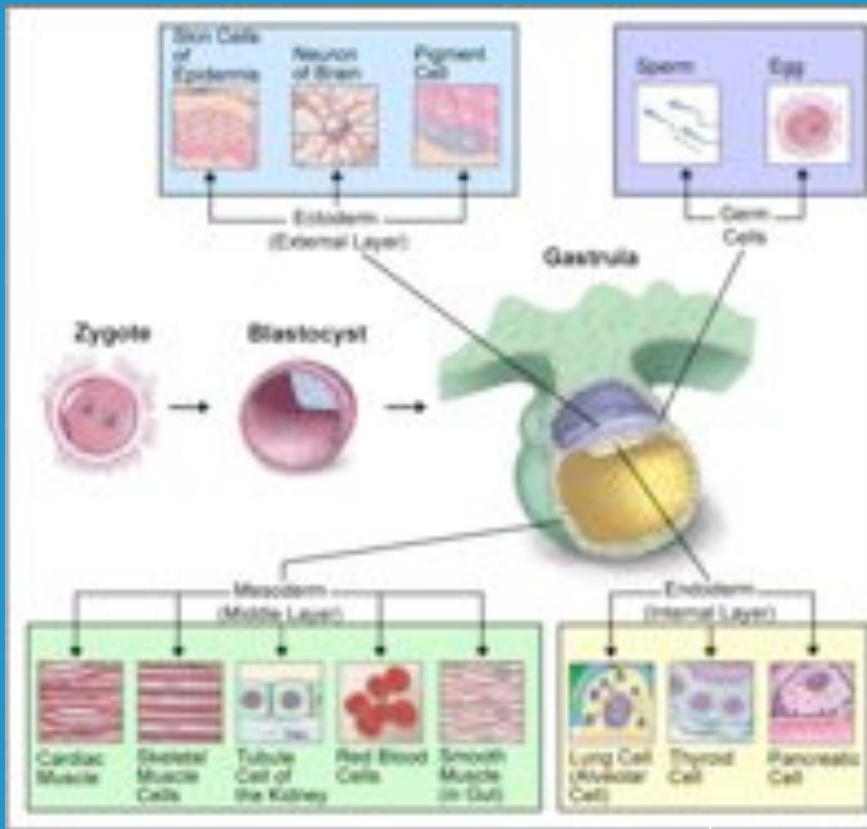
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# Outline

- **You will each be allocated a question**
- **Work in pairs to “brainstorm” each question for 10 minutes before we go through each in turn**
- **I will give some clinical examples!**

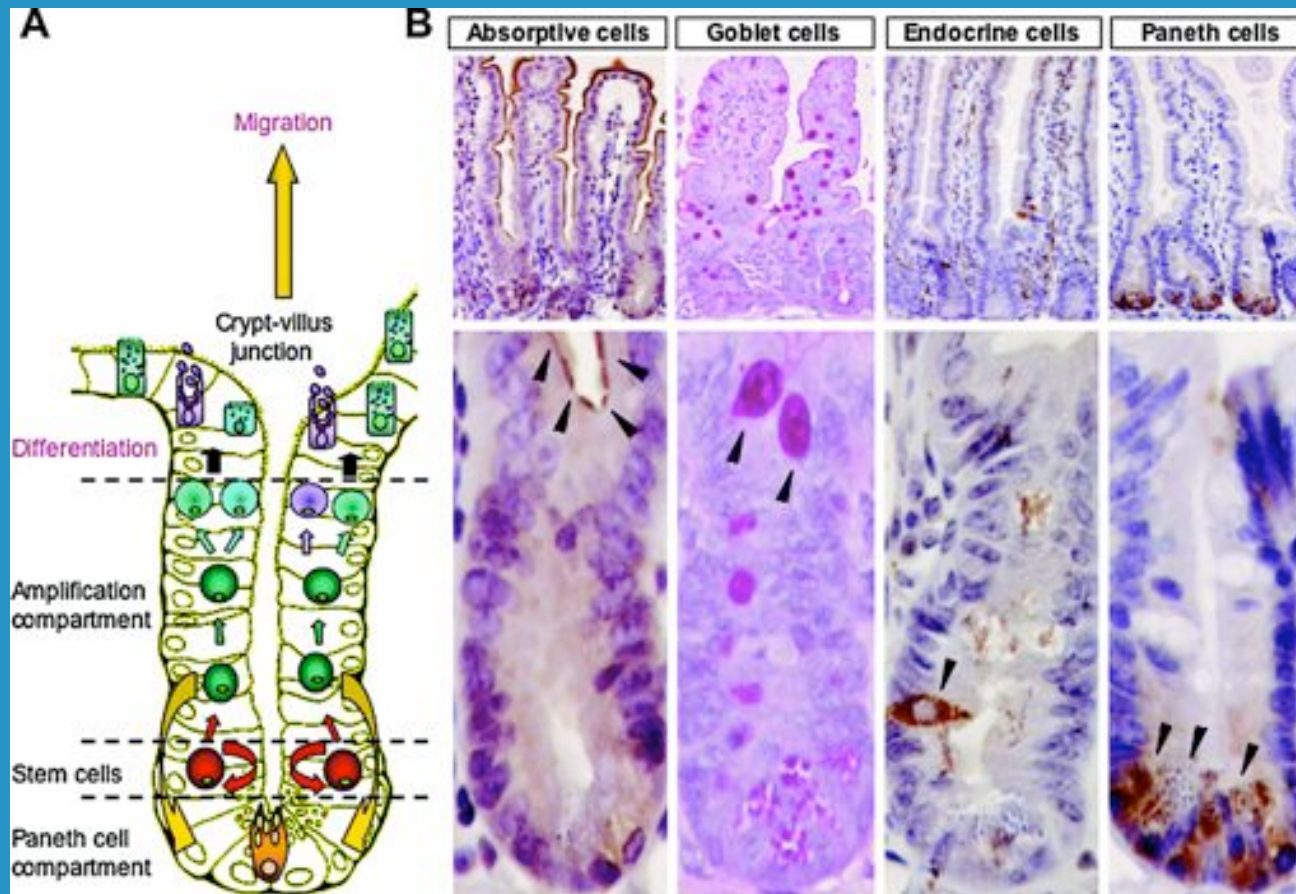
# 1- What are the various factors that regulate the number of cells in a tissue?



And gut!

- **Balance between proliferation, differentiation and cell death**
- **Totipotent cells (zygote)**
- **Pluripotent “stem cells” can differentiate into many cell types**
- **Multipotent stem cells in adult organs/tissue replenish specialised cells**

# Regulation of cell number in the intestinal crypt



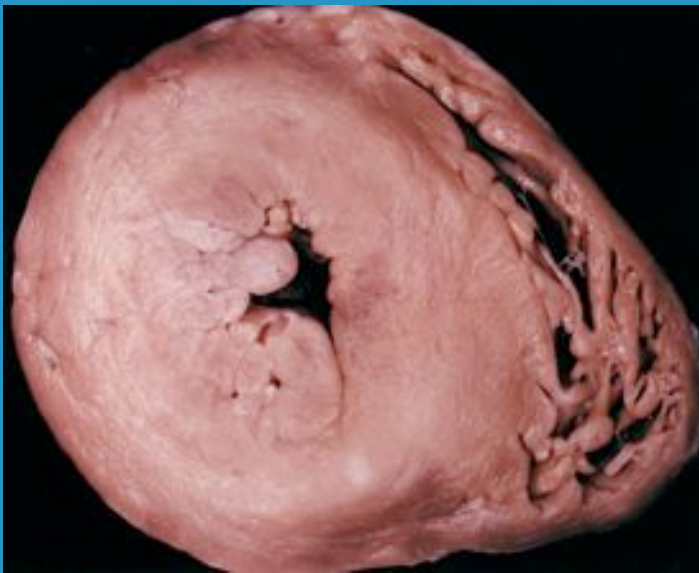


## **2- Can you define the following terms?**

- **Hypertrophy**
- **Hyperplasia**
- **Atrophy**
- **Metaplasia**
- **Dysplasia**
- **Neoplasia**

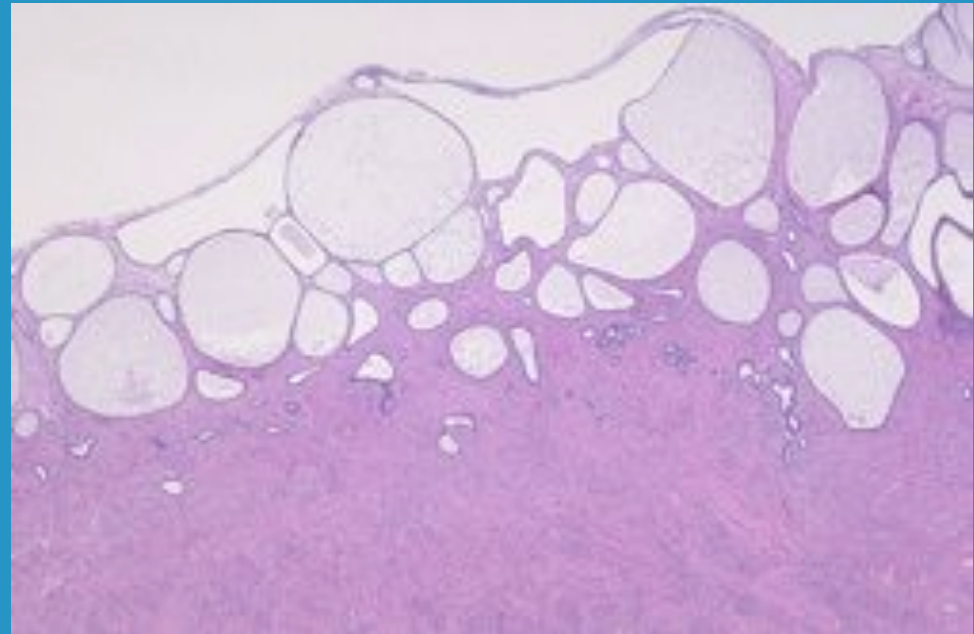
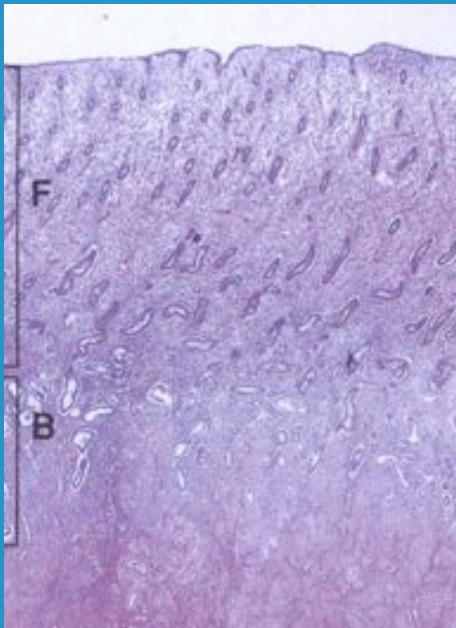
# Hypertrophy

- **Reversible increase in size of whole or part of an organ or tissue by increase in cellular size but not number**



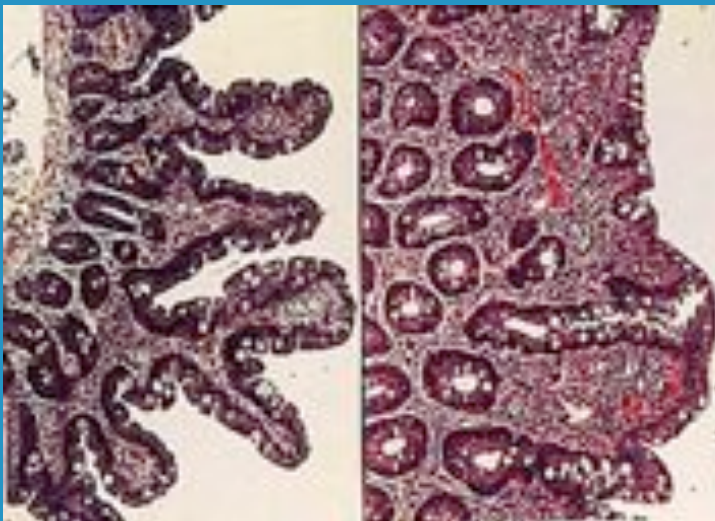
# Hyperplasia

- **Increase in size due to increased number of cells eg. BPH, endometrial hyperplasia**



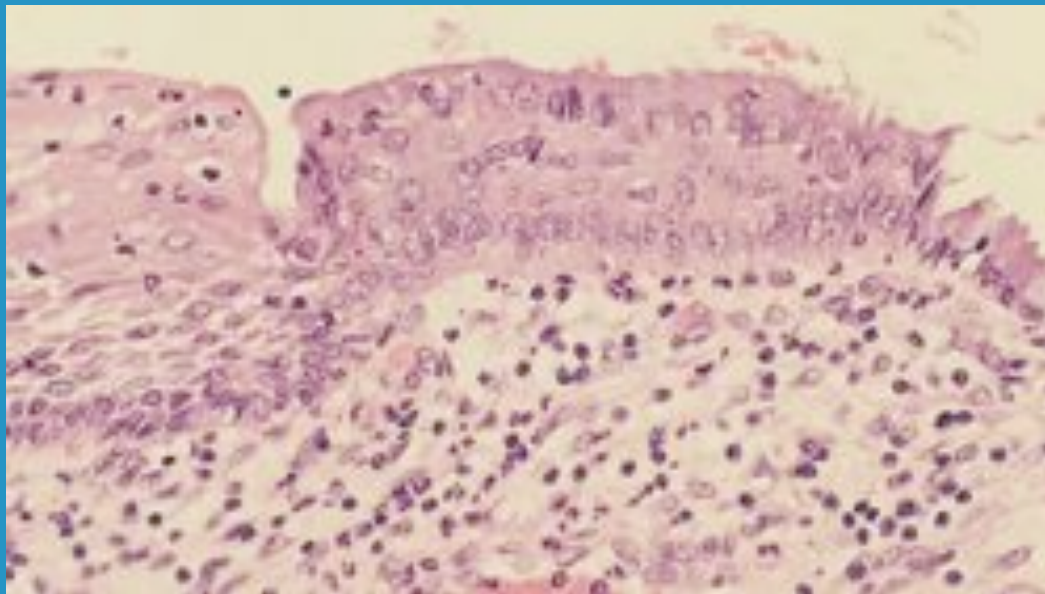
# Atrophy

- **Decrease in size due to reduction in cell size and or number**
- **Multifactorial (growth factors, hormones, inflammation etc)**



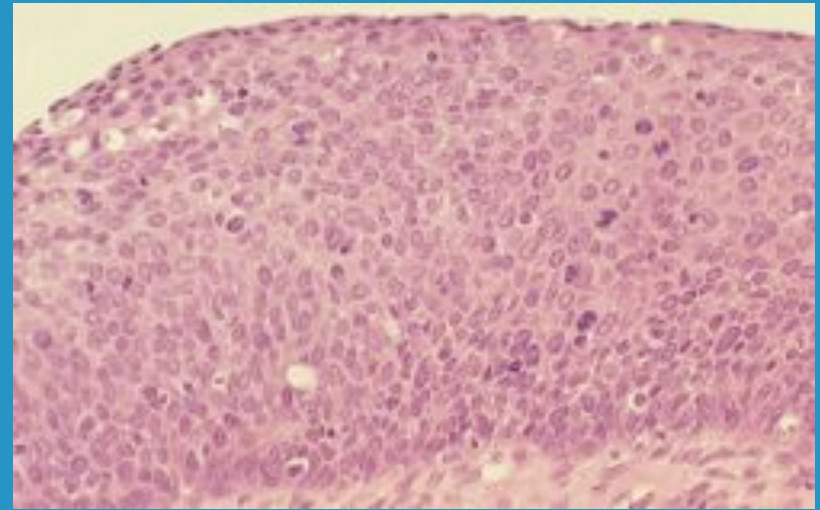
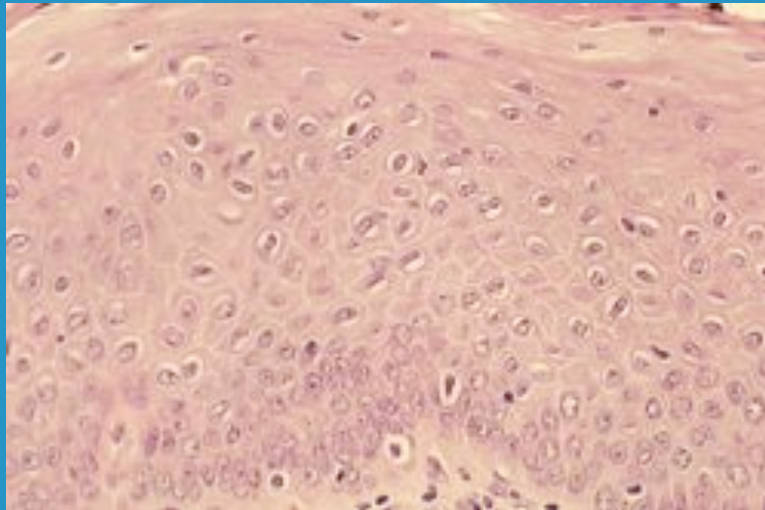
# Metaplasia

- **Reversible change of one differentiated cell type to another e.g. smoker's respiratory epithelium, cervix "transformation zone", Barrett's oesophagus**



# Dysplasia

- **“bad form” in Greek**
- **Common term for pre-cancerous lesions**
- **Abnormal cells with architectural and cytological abnormality but no invasion. Severe dysplasia also called “carcinoma in situ”**

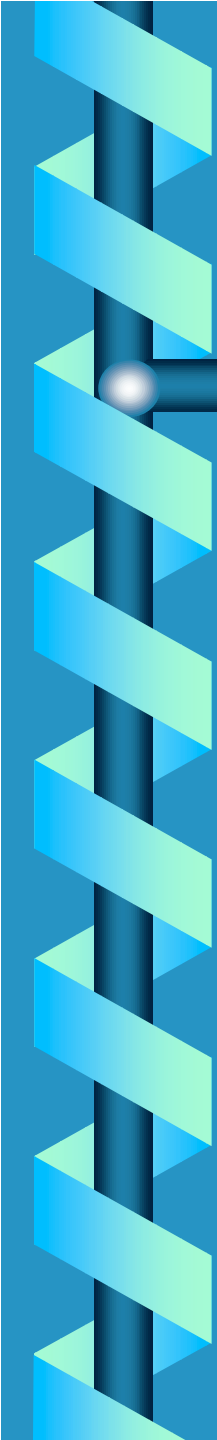




# Neoplasia

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- **Literally “new growth”**
- **Abnormal disorganised growth in a tissue or organ usually forming a distinct mass**
- **Refers to both benign and malignant tumours**

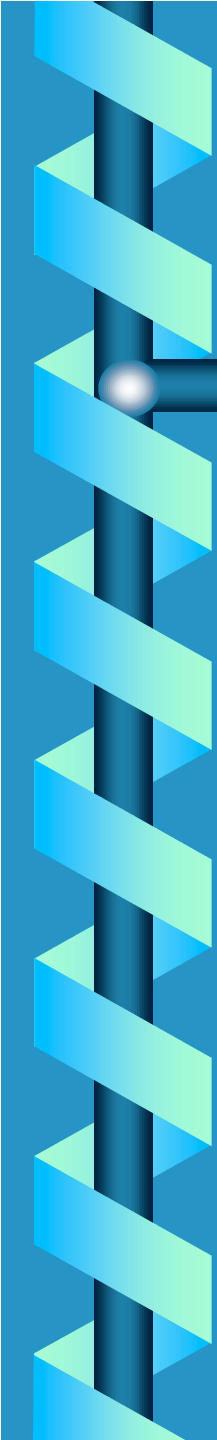


### **3- What is the value of having knowledge of epidemiology of neoplasia?**

- **Epidemiology can point to aetiology and risk factors**
- **Common and rare cancers**
  - **Planning of health care provision**
  - **Screening and prevention**
  - **Identify genetic factors and “at risk groups”**

## **4- How can we broadly classify different neoplasms?**

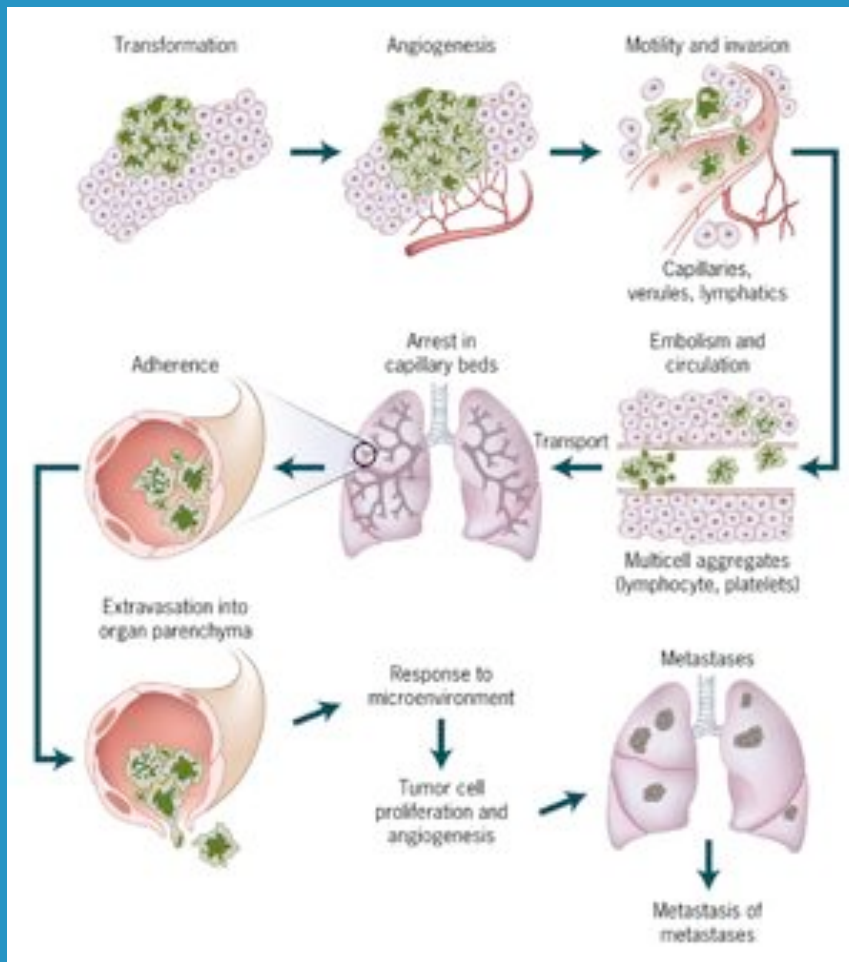
- **Anatomical classification**
  - Lung tumours, breast tumours
- **Histogenetic**
  - Based on presumed cell of origin
  - Carcinoma, sarcoma, lymphoma
- **Behavioural classification**
  - Based on likely behaviour / aggressiveness (malignant potential)
  - What are the main differences between benign and malignant tumours?



## **5- What do the terms “grade” and “stage” mean and what is their clinical significance?**

- **Grade**
  - **How well does the cancer resemble normal tissue?**
  - **Low grade = well differentiated**
  - **High grade = poorly differentiated**
- **Stage**
  - **Extent of spread (TNM most common)**
- **Both influence prognosis and treatment (MDT meeting)**

# 6- What are the key events in process of metastasis?



1. Local growth
2. Angiogenesis
3. Altered cell motility and cell-cell interactions
4. Altered ECM
5. Invasion of lymph / blood vessels
6. Survival in vessels
7. Arrest at distant site
8. Survival at distant site
9. More local growth and repeat cycle

# 7- In what ways do neoplastic cells differ from normal cells?

- **Appearance of cells**
  - Increased nuclear to cytoplasmic ratio and nuclear pleomorphism
  - Darker nuclear staining (hyperchromasia)
- **Genetic / Biochemical changes**
  - Altered chromosomal / DNA content (aneuploidy and mutation of key regulatory genes)
  - Altered antigen expression (evade immunity)
- **Behaviour of cells**
  - Immortality in cell culture (no senescence)
  - Loss of contact inhibition and anchorage independence
  - Form tumours in animals

## **8- What lines of evidence suggest cancer is a genetic disease?**

- **Cancer increases according to the sixth power of age**
- **Some cancers run in families**
- **Germline mutations lead to early and sometimes multiple cancers**
- **Carcinogens alter DNA sequences (mutagens)**
- **Tumour cells show mutations and chromosomal changes, some of which are characteristic of certain cancers (9;22 in 95% CML cases)**

# Familial Adenomatous Polyposis



# 9- How do neoplasms present clinically?

- **Local**
  - SOL, compression, ulceration, bleeding, invasion local structures
- **Systemic**
  - As above
- **Paraneoplastic**
  - Anaemia, electrolyte disturbance, inappropriate hormone production, skin changes, dermatomyositis etc.
- **Incidental finding**
  - Screening (“incidentalomas”)



# 10a- What are oncogenes?

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# Oncogenes

- **A proto-oncogene is a gene involved in growth regulation that can become an oncogene after mutation or overexpression**
- **Oncogenes are genes that increase the malignant potential of a cell**
- **Oncogenes were first discovered in animal viruses**



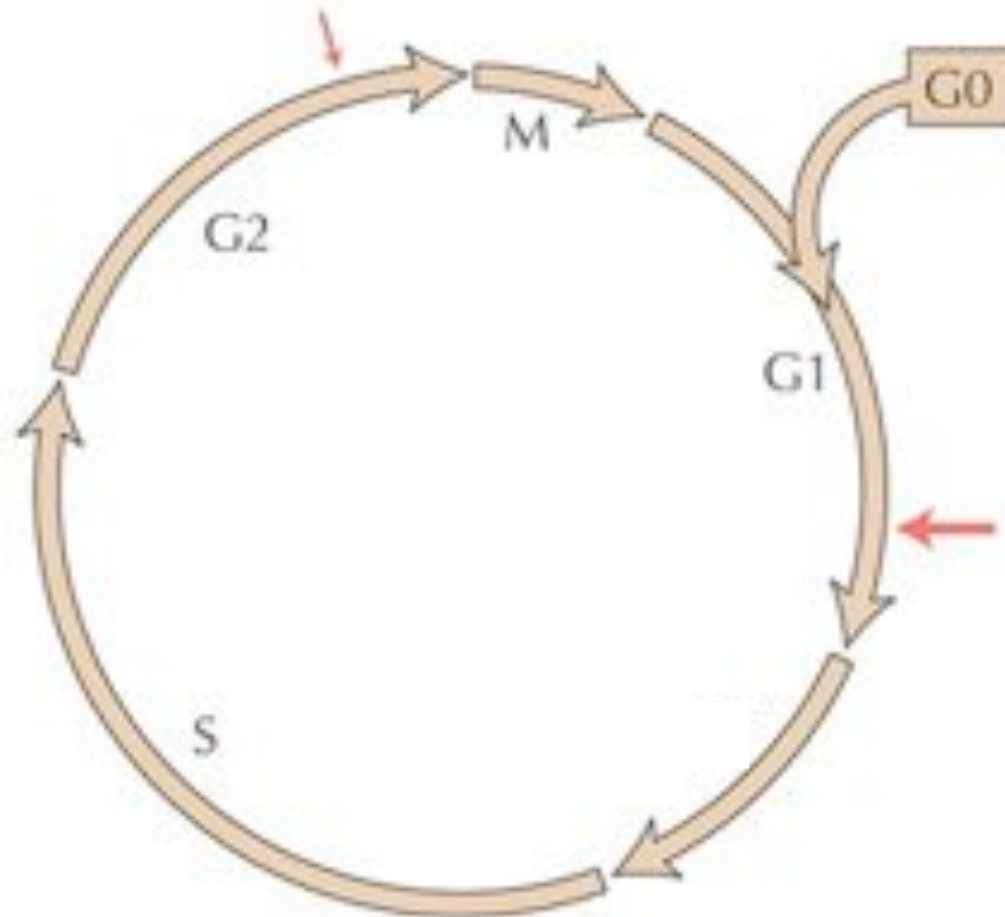
# **10b- What are tumour suppressor genes?**

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# **Tumour suppressor genes**

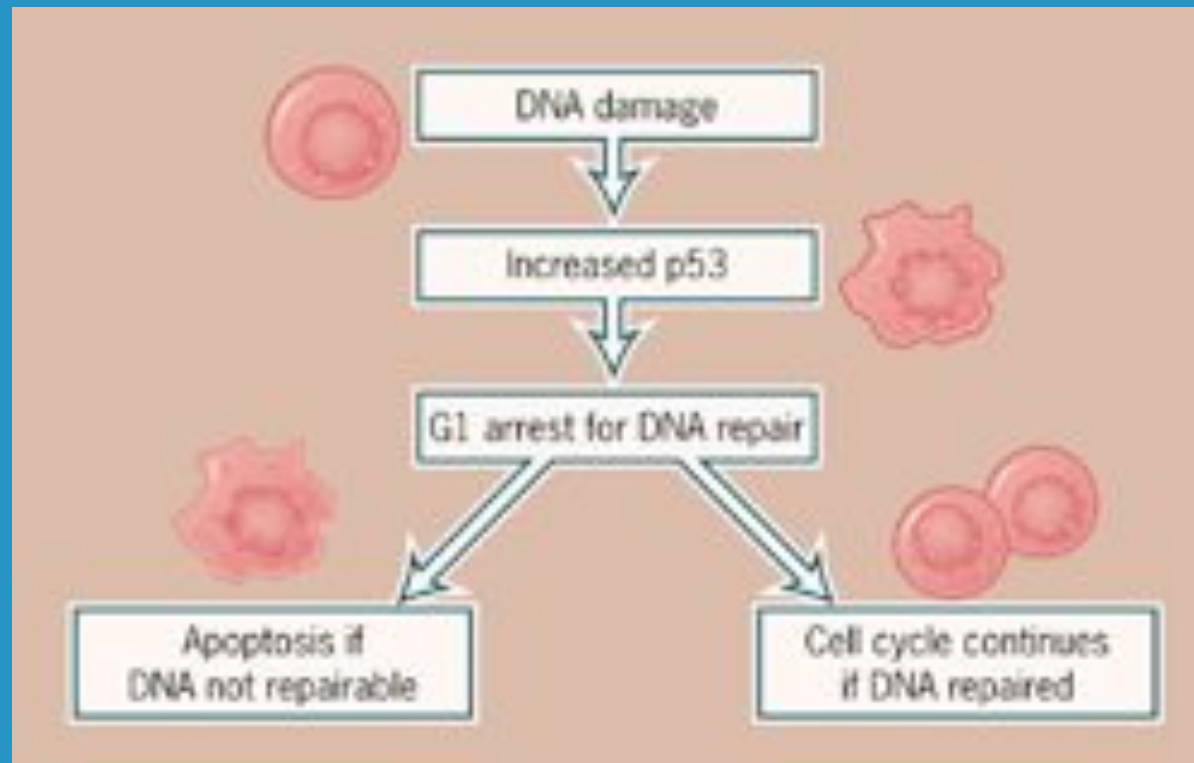
- **These are genes that normally act as “brakes” on cell proliferation or which normally promote cell differentiation or apoptosis**
- **Deletion or inactivation of TSGs increases cell malignant potential**
- **Inactivation of both copies of a TSG is normally required for this (“two hit hypothesis”)**
- **Alteration of proto-oncogenes and TSGs are needed for development of malignant tumours**

# 11- What are the stages of the cell cycle and what are checkpoints?

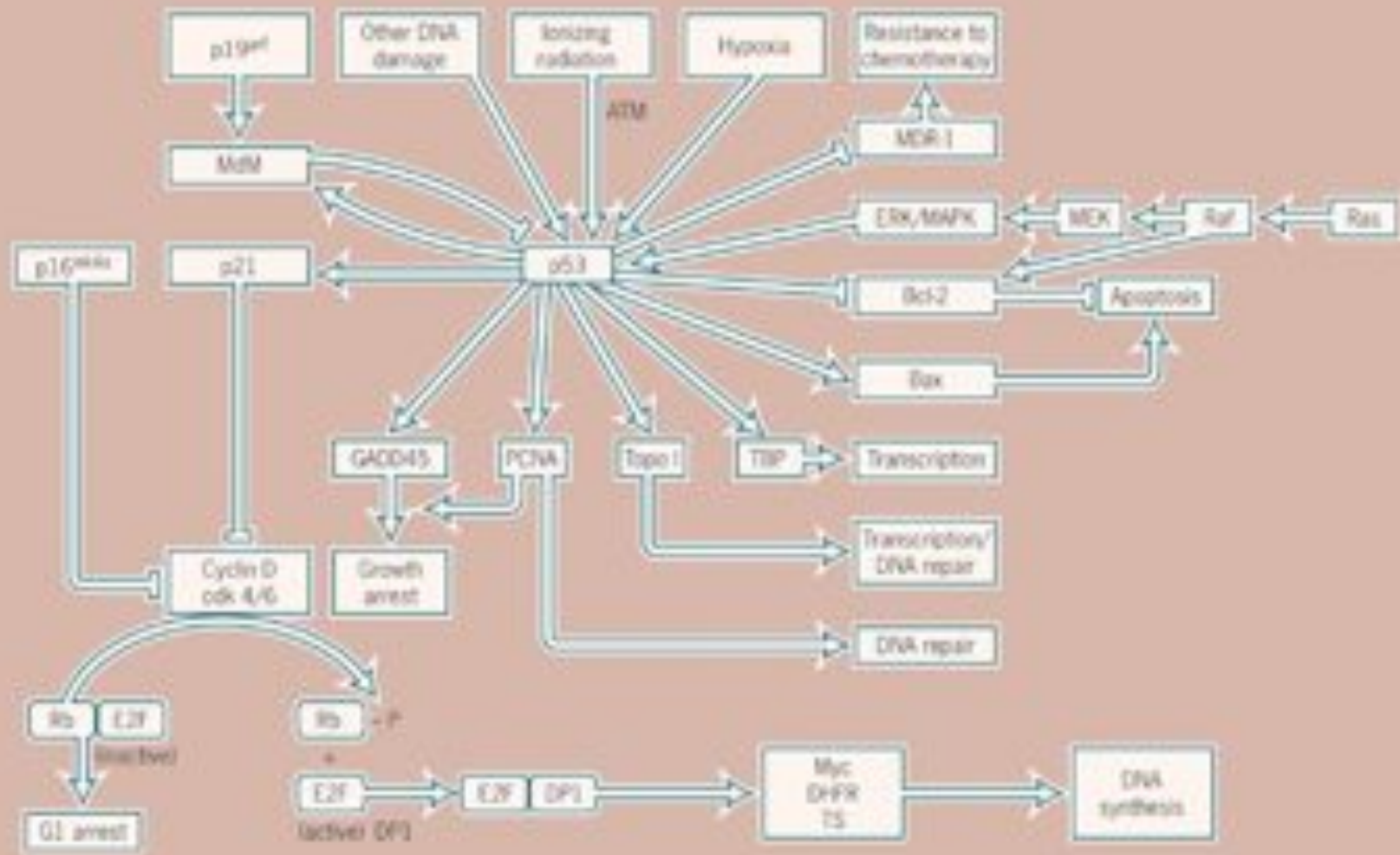


# 12- What is p53 and how does it work?

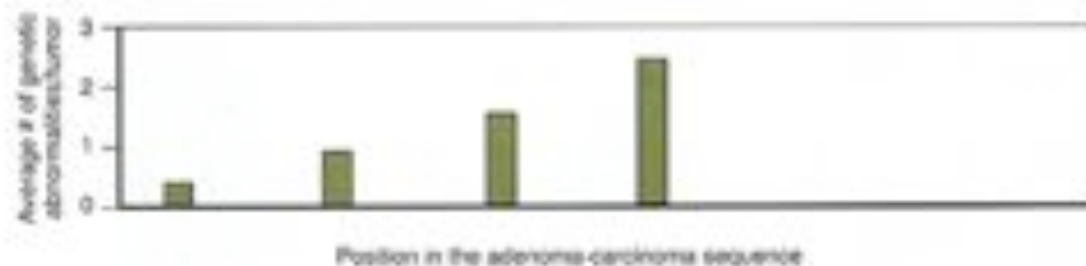
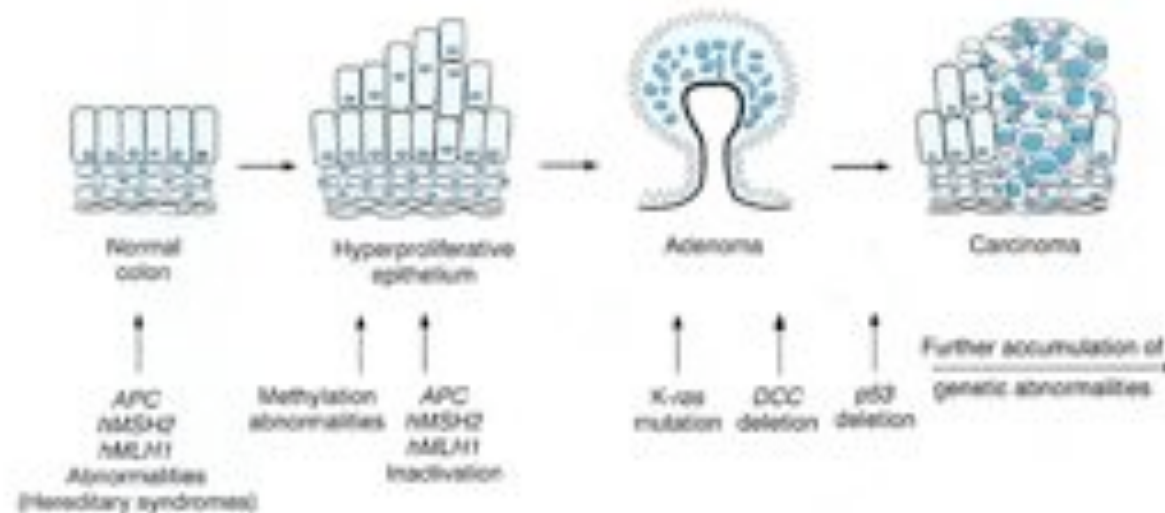
- TSG altered in at least 70% cancers



# p53 “master controller”



# 13- What are the molecular events that occur in the genome of neoplastic cells to escape normal growth control?





# Questions?

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