

Cancer – Summary

(From Organisation and Control of Prokaryotic and Eukaryotic Genome)

Tumorigenesis: Uncontrollable cell growth

Malignant tumours:

- Invasive - erodes normal surrounding tissue
- Metastatic - can migrate to other parts of the body for clonal expansion

Primary tumour → metastasis → secondary tumours

Natural selection at work: fittest cancer cell survives

Begins with genetic changes → non-cancerous benign tumour → malignant tumour

Most cancers originate from a single aberrant cell

e.g.:

1. Cells grow as benign tumour in epithelium
2. Break through basal lamina
3. Invade capillary
4. Adhere to vessel wall in liver
5. Escape from blood vessel (extravasation)
6. Proliferate

Detailed Development:

1. Cell proliferation controlled at many checkpoints. All of these controls have to mutate to initiate cancer.
2. At least 5- 6 mutations in critical genes must take place before cell turns cancerous.
3. Combinations of such mutations much confer some growth advantage to the cell. E.g.:
 - a. Become increasingly unresponsive to normal cell proliferation control
 - b. Able to generate new blood vessels for nutrients
4. Multiplicity explains why cancer is relatively rare during an average human lifetime.
5. Cause of cancer are multifactorial:
 - a. Environment
 - b. Diet
 - c. Lifestyles
6. Entire process from normal to cancerous cell can take 10-20 years.

Critical Genes:

- Proto-oncogenes
 - Products promote cell growth
 - E.g.:

- Growth factor
 - Growth factor receptor
 - Growth signal transduction factors
 - Transcriptional factors
- MUTATED form → oncogenes
 - Gain of function mutations
 - Enhance cell function and thus tumorigenesis
 - Via:
 - Retroviral integration
 - Missense mutation
 - Gene amplification
 - Chromosomal translocation
- Tumour Suppressor Genes
 - Products inhibit or slow down cell division
 - Thus preventing cancerous growth
 - Loss of function mutations
 - Leads to inactivity or decreased activity
 - Thus promoting tumorigenesis
 - Mutations are usually recessive
 - Both copies need to mutate or be deleted
 - Since the other one that functions normally serves as backup
 - Classic example – p53:
 - Most commonly altered in human cancers
 - About 50% of human cancers associated with defects in this gene
 - Plays important when there is DNA damage:
 - DNA cell repair
 - Cell arrest
 - Initiates apoptosis
 - Defective p53 protein enables the propagation of cell cycle such that cell growth and division continues with the damage. The damaged DNA will replicate and risk of developing cancer cells is increased.
- Just remember: LOSS IN FUNCTION vs GAIN IN FUNCTION