Cancer

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Tags	

Explaining how lack of control of cell division can result from changes in expression of tumour suppressor genes/porto-oncogene

COMMON MISTAKES:

- Question is asking how uncontrolled cell division is caused by decreased protein production meaning that protein still functional but less
- Question not asking how lack of controlled cell division can lead to **cancer** (cancer is needed to be able to mention gain in function or loss in function mutation

▼ Tumour suppressor genes

- Decrease in expression of tumour suppressor genes
- Ref to named example (p53)
- Result in fewer proteins (NOT DEFECTIVE PROTEINS) that inhibit cell division/ arrest cell cycle at checkpoints/ promote DNA repair/ promote apoptosis
- Cell would continue to divide/not undergo apoptosis even in presence of irreparable DNA damage
- As mutations accumulate and cell survives through many divisions, uncontrolled cell division may occur

▼ Porto-oncogenes

- Increase in expression of porto-oncogenes

- Ref to named example (ras)
- Would result in more proteins that stimulate normal cell growth and cell division/inhibit cell differentiation/halt cell death
- Cell would divide excessively

Explain how mutations affecting the two groups of genes involved in cell cycle regulation may lead to development of cancer

Definitions

- Gene mutations occur when an insertion, deletion, substitution of bases lead to a change in nucleotide sequence of a gene
- Chromosomal aberration can be in the form of a change in structure of chromosomes or number of chromosome due to failure of sister chromatids to separately during anaphase I and II failure of homologous chromosomes to separate properly in anaphase I, resulting in non-disjunction
- Proto-oncogenes code for proteins that stimulate cell division
- Tumour supressor genes code for proteins that inhibit cell division

Proto-oncogenes

- A gain of function mutation to proto-oncogenes such as Ras to give rise to oncogene causing the product coded for by the gene being hyperactive or produced im excess such as growth factors or promote progression of cell cycle
- A mutation of one of the two copies of proto-oncogene into an oncogene is sufficient to cause abnormal cell proliferation
- A proto-oncogene can be may be moved from its normal location in one chromosome to another, and be placed under the control of enhancers/ a more active promoter which stimulates cell division
- translocation where a section of chromosomes breaks off and attaches to a non-homologous chromosome

- A point/gene mutation can occur in the promoter/ enhancer /silencer that controls proto-oncogene causing an increase in expression
- A point/ gene mutation can occur in the coding region/sequence/exons of the proto-oncogene, altering 3D conformation of the protein coded for such that it is hyperactive and resistant to degradation

Tumour suppressor gene

- A loss of function mutation may occur to the tumour suppressor gene such as p53, resulting in the product coded for by the gene being non-functional or reduced in expression
- Both copies of tumour surpressor gene need to be mutated so that no functional gene product Can be reduced resulting in abnormal cell proliferation
- transloaction can occur where a section of a chromosome breaks off and attaches to a non-homologous chromosome
- A tumour suppressor gene could be moved and placed under the the control of silencers or less active promoter where a repressor will bind to resulting in lack of expression of its gene product which inhibits cell division
- Deletion involves the loss of section of the chromosome andThe possible loss of tumour suppressor genes in the deleted section will lead to lack of expression of its gene product which inhibits cell division
- Inversion occurs when a segment of nucleotide sequence of the tumour surpressor gene being read on the reversed manner resulting in a different mRNA sequence resulting in the formation of non-functional tumour suppressor protein to inhibit cell division, initiate DNA repair and promote apoptosis
- A point/gene mutation can occur in the coding region/sequence/ exons of a gene, altering the 3D conformation of the protein coded for resulting in a non-functional protein
- A point/gene mutation can occur in the promoter/ enhancer /silencer that controls proto-oncogene causing an increase in expression

- As a result, it is unable to stop cell cycle to allow repair any damaged DNA, unable to activate DNA repair mechanism to repair damaged DNA thus accumulation of mutations occurs, unable to initiate apoptosis thus cell potential to cause cancer is not removed (role of tumour suppressor genes can lead to cancer)

Development of cancer (why is cancer development a multi-step process)

- Cells with mutations bypass / not arrested at the cell cycle checkpoints / do not undergo apoptosis, giving rise to daughter cells with mutations
- Accumulation of mutations occur in a the genes of a single cell, Including at least one gain-of-function mutation in an allele of at least one proto-oncogene to oncogene causes excessive protein to form tumour, results and loss-of-function mutations in both alleles of several tumour suppressor genes causes further dysregulation of cell cycle to have excessive tumour And in other cancer-critical genes such as genes controlling anchorage dependence, able to travel new location /contact inhibition causing cancer cells to pile on each other / angiogenesis, forming new blood vessels to enable cancer cells to spread to other sites of the body / metastasis / coding for telomerase to lengthened and able to divide indefinitely leading to uncontrolled cell division;
- Cancer cells may spread to other locations distant from their original site in the body via lymph vessels or blood vessels, and form secondary tumours in a process known as metastasis;

Describe the change in the basal layers when cancer is developed

- Infected cells in basal layer are mutated to become precancerous cells which are irregular in size and shape
- Epithelial cells lose contact inhibition (when they come into contact with other cells they usually stop dividing but cancer cells don’t, piling on top of each other) forming disordered multi layered patterns. as it differentiates and progress to the surface of the epithelium, number of infectious virus parts increases and they eventually released from the precancerous epithelial cells
- Cell divide in uncontrolled manner, breaking through membrane and dermis and mestatising to other areas, developing invasive cancer

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Describe how dysregulation of the checkpoints of cell division may lead to cancer

- M checkpoints: any chromosomes not attached to spindle fibre synthesise, cell continues into metaphase and anaphase to produce genetically altered cell
- G1/G2: damaged DNA not repaired and cell continues in M phase, accumulating cell mutations, uncontrolled cell division that leads to tumour

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Describe the process of angiogenesis and explain its importance in the development of cancer

- angiogenesis is the process of forming new blood vessels in response to chemical signals given off by tumor
- Blood vessels transport blood with oxygen and nutrients to tumour
- Helps for cell growth and cell division and hence potential unlimited growth of the tumour
- Blood vessels also provide a route for tumour cells to metastasis's to other parts of body to form secondary tumour
- Resulting in a malignant cancer