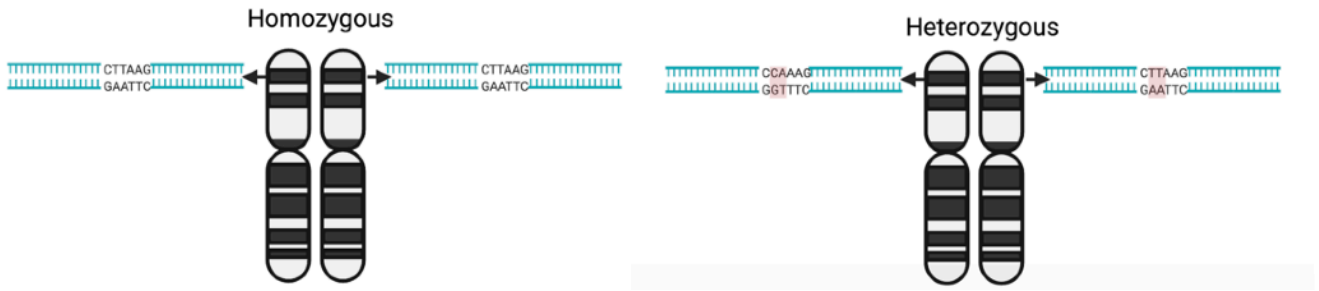
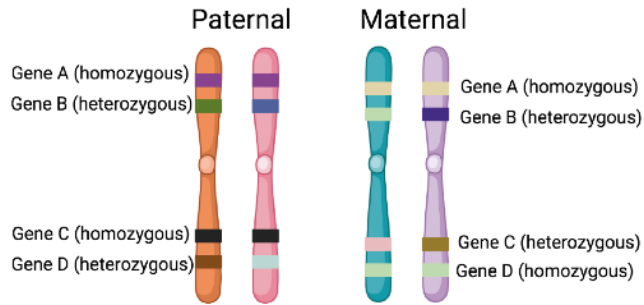


Question 1

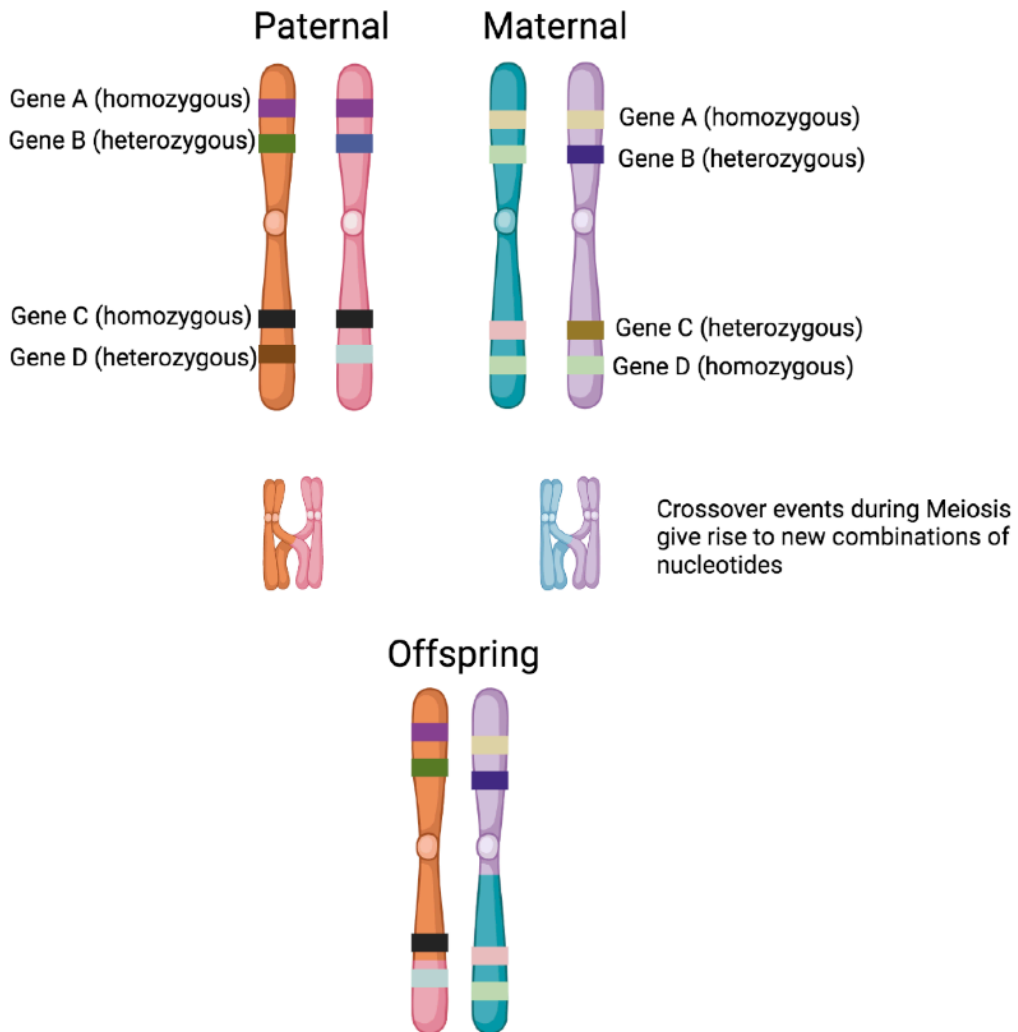
1.1



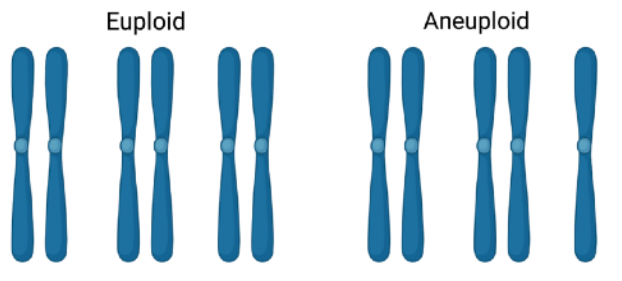
1.2



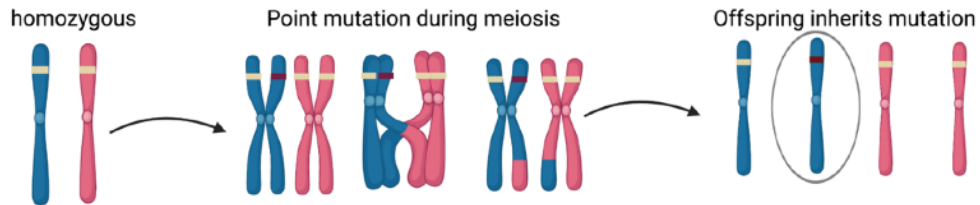
1.3



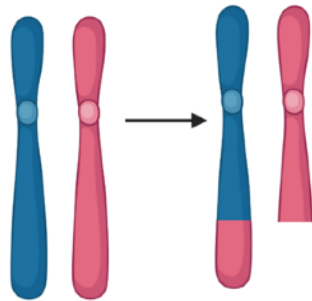
1.4



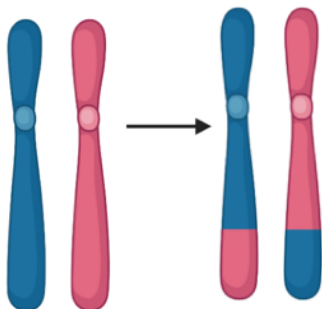
1.5-



1.6



1.7



1.8 Normal morphology refers to cells or tissues that are functioning as expected. Abnormal morphology refers to some kind of abhorrent activity that is not expected for that cell/tissue.

1.9 The ECM is a network of proteins and other molecules that scaffold and provide support to cells. Some important proteins include collagen, elastin, fibronectin, and laminin. Proteoglycans

also play an important role in the function of the ECM. In normal tissues the ECM can supply cytokines and growth factors, and can provide physical structure and cues.

1.10 Cell-cell contacts are physical interactions between cells. Cadherins mediate these interactions in epithelial cells.

1.13 A fully differentiated cell has a specific morphology, function, and gene expression pattern based on the cell type. Differentiated cells give rise only to differentiated cells. Progenitors are less differentiated and can give rise to several related cell types, whereas stem cells can be even less differentiated and give rise to a wider variety of cell types.

1.14 One type of epigenetic modification is methylation, which is the addition of methyl groups onto the tails of histones. Histone tails can also be modified with acetyl groups - acetylation.

1.15 Phosphorylation: addition of a phosphate group. Methylation: addition of a methyl group. Acetylation: addition of an acetyl group. Hydroxylation: oxidation of a C-H bond to C-OH. Glycosylation: addition of sugars. Ubiquitination: addition of the small protein ubiquitin.

1.16 Transphosphorylation is the transfer of a phosphate group between two compounds.

Question 2

2.1 Hyperplasia refers to an increase in cells which appear normal. Dysplasia refers to abnormal but non cancerous cells. Neoplasia is benign or malignant abnormal cell growth.

2.2 Stroma is the supportive and connective tissue including blood vessels, nerves, and ducts. some cell types often found in the stroma include fibroblasts, pericytes, endothelial cells. adipocytes, and mesenchymal stem cells.

2.3 The main roles of epithelial cells in the breast are to line ducts and lobes, and produce milk. Myoepithelial cells perform a contractile function during lactation and contribute to the production of proteins for the basement membrane, and fibroblasts contribute to the connective tissue and stroma which supports other cell types.

2.3 (2) Invasive tumors spread to nearby tissues from their original origin. Metastatic tumors spread outside the original tissue to other distant locations. Benign tumors do not spread to other areas.

2.4 A primary tumor is the original tumor site, a recurrence is a tumor re-forming in the same or similar location.

2.5 This could be true since the tissues are closely located. If the secondary site is close to the original, this may be the result of an invasive tumor. If the locations are more spaced apart and the recurrence results from spread of cancer cells through blood vessels or lymph, this could be the result of a metastatic tumor.

2.6 A cell of origin is the first transformed cell which carries cancer causing mutations.

2.7 Sarcoma: cancer of connective tissue. Carcinoma: cancer of epithelial tissue. Lymphoma: cancer of lymphatic tissue. Blastoma: cancer of precursor cells. Glioma: cancer in the brain/spinal cord of glial cells.

2.8 An adenoma is an epithelial glandular tumor that is benign. Adenocarcinoma is a type of carcinoma that occurs in glands.

2.9 The basement membrane is a layer of extracellular matrix composed of substances such as glycoproteins and laminins that lie under epithelial cells and endothelial cells and surround fat, muscle, and some glial cells. Basement membranes can act as a barrier to tumor invasion. In the breast, basement membrane would provide physical and biochemical support to epithelial cells, fat cells, muscle cells, and endothelial cells. The basement membrane is part of the ECM.

2.10 Dedifferentiation means a cell becomes less differentiated - it reverts to a less specialized cell.

2.11 A compound which is metabolized into a carcinogen.

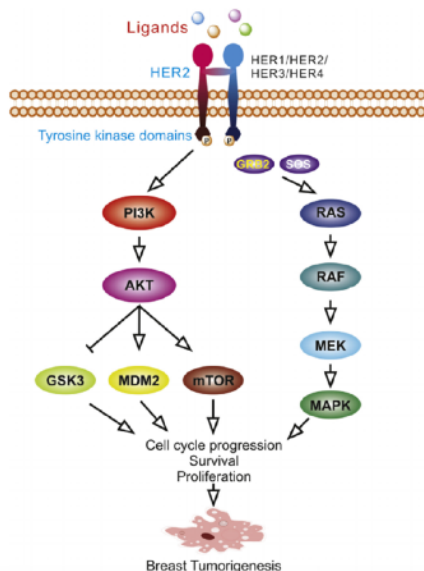
2.12 A proto-oncogene is a gene which may cause the cell to become cancerous if mutated. Oncogenes are mutated genes which may cause cancer. The same Principle applies to proteins: proto-oncoprotein is a protein which may cause cancer if mutated, and an oncoprotein is a mutated proto-oncoprotein.

Question 3

Monoclonality refers to tumors which are derived from a single transformed cell. Polyclonal tumors are derived from two or more cells which transformed individually. It is believed that tumors are generally monoclonal.

Question 4

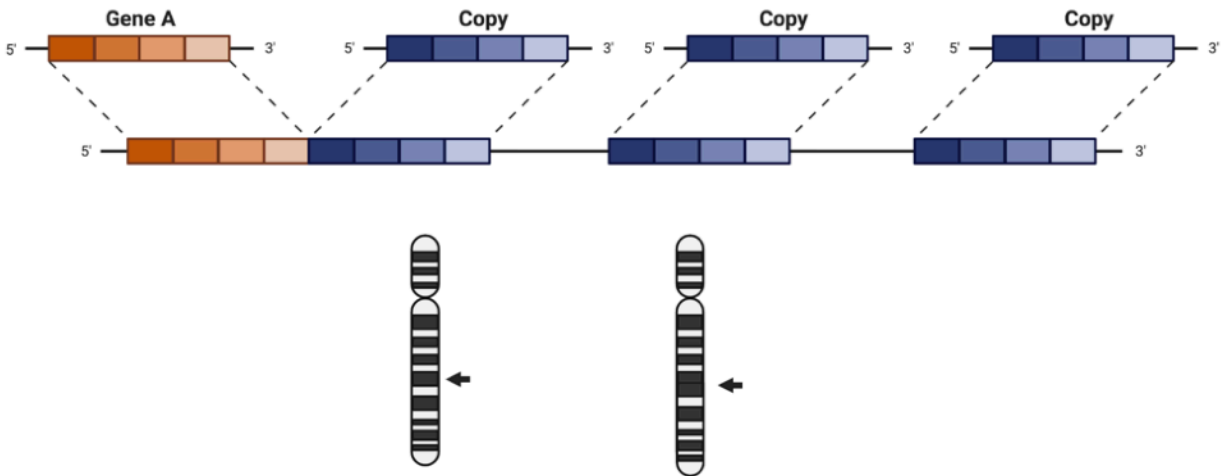
- HER2 is a tyrosine kinase receptor
- HER2 is normally expressed in epithelial cells
- HER2 is involved in signalling pathways including mitogen-activated protein kinase (MAPK) and phosphoinositide 3-kinase (PI3K/Akt) phospholipase C γ



DOI:10.1016/j.gendis.2018.05.001

-HER2 is a proto-oncogene in breast and ovarian cancer

-All amplifications may not be the same. There can be amplifications of different stretches of DNA, including protein coding genes, promoters, and other regulatory sequences.



-amplification of a proto-oncogene can cause it to become an oncogene by increasing activity. Having a much larger amount of HER2 in the cell as a result of expression of multiple copies can deregulate its activity

Question 5

This is because the cell is producing its own signalling molecules. Cells being in charge of their own growth factors presents a high risk of deregulation since the signalling loop is contained to that cell, whereas when multiple cell lines are involved in a signalling cascade there are more barriers preventing deregulation of the pathway.

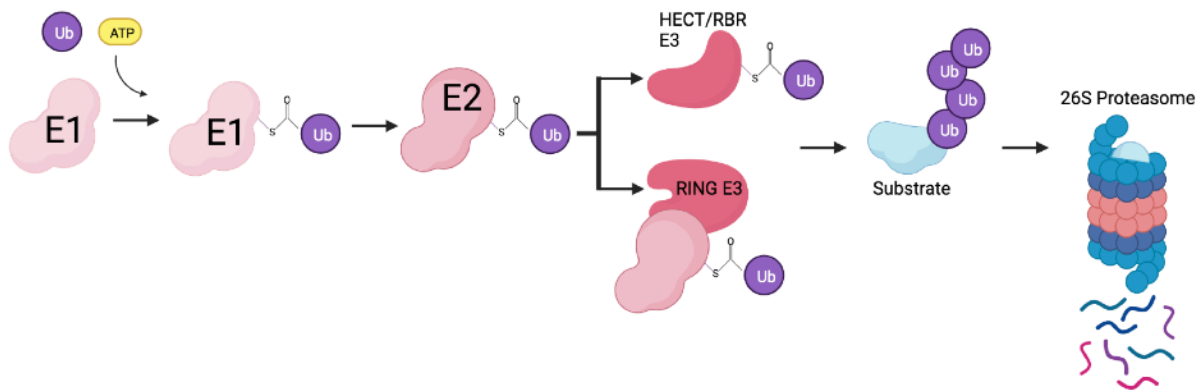
Question 6

In many signalling pathways, there are negative controls in place in order to prevent abhorrent activation. Negative feedback can reduce a cells responsiveness to a signal even when the signal has not reduced in magnitude.

Question 7

Ubiquitin is a small protein which has many cell signalling implications when ligated onto proteins depending on the ubiquitination site, the number of ubiquitins in the chain, and the type of linkage between ubiquitins in the chain. Chains of at least four ubiquitin linked at K48 or K63 ligated to a protein substrate recruit the 26S proteasome to degrade the ubiquitin labeled protein. Ubiquitin is ligated onto these substrates by a series of enzymatic steps. E1 enzymes

such as Uba1 activate ubiquitin in an ATP dependent process, forming a thioester intermediate. The activated ubiquitin is then transferred to form a thioester with an E2 ubiquitin conjugating enzyme such as UbcH7. The ubiquitin will then either be transferred onto the catalytic cysteine of an E3 enzyme (for HECT or RBR E3 ligases), or the E3 will act as a scaffold for ubiquitin to be transferred from the E2 onto the substrate (RING E3 ligases).



Examples from the literature will vary but should include ubiquitination signalling proteasomal degradation.

Question 8

The most obvious answer is no, since these concepts are inherently conflicting. If no, the student should provide explanation as to why these two outcomes could not arise simultaneously from one gene. If yes, examples should include plausible explanation of how one gene could act as both an oncogene and tumor suppressor. Students should provide a scenario in which amplification/overexpression/constitutive activation of a gene or gene product could promote oncogenesis AND deletion/ decreased expression/ inactivation of the gene or gene product could promote oncogenesis.

Question 9

Severely shortened telomeres can initiate crisis, prevent cell division, and signal for senescence or apoptosis. However, shortened telomeres can also create genomic instability. This increased mutational rate can provide an opportunity for advantageous mutations to arise, and for tumor evolution. However, if telomere shortening is never addressed the insult of DNA damage would likely result in cell death.