Full Name:	Civics group: 21S	Index no.:	Date:

Core Idea 2: Genetics and Inheritance

Molecular Biology of Cancer

Tutorial 11

Question	1	2	3	4	5
Answer	D	D	D	B	C

1 Which of the following contribute(s) towards cancer progression?

1 Activation of genes that causes cell death.
2 Inactivation of genes that slow down the cell cycle.
3 Activation of genes that result in growth of new blood vessels.
4 Inactivation of genes involved in cell-cell adhesion.

A 2 only
B 1 and 3
C 1 and 4
D 2, 3 and 4

2 Which of the following is **not** true about cancer cells?

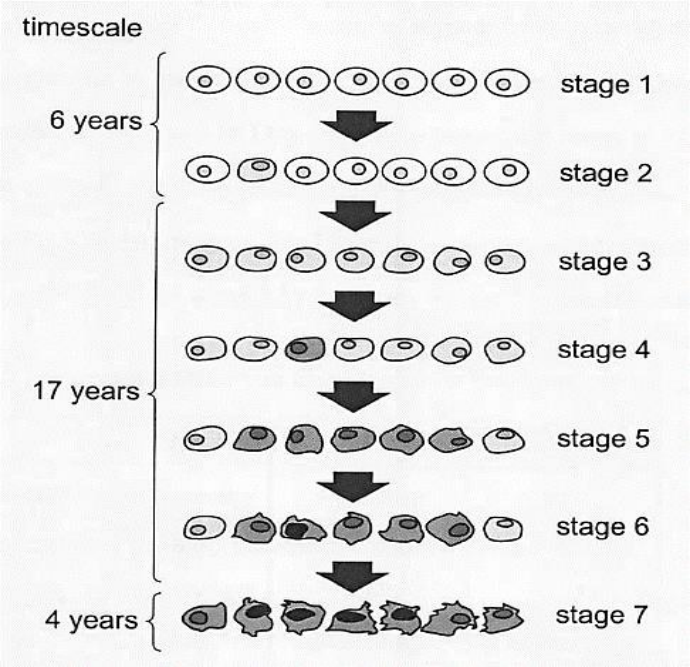
A Metastasis establishes new tumours distant from the site of the primary tumour. Metastasis establishes secondary tumours

B Telomerase maintains the length of telomeres, allowing for continuous cell division. Enzyme lengthens telomeres, using a RNA template. NB: End-replication problem still occurs.

C Angiogenesis forms new blood vessels and brings nutrients and oxygen to the tumour. Formation of new blood vessels also allows waste products to be carried away from rapidly dividing cells.

D Cancer cells exhibit anchorage dependence. Cancer cells do not exhibit anchorage dependence, therefore they can dislodge from original tumor and undergo metastasis.

3 The diagram represents stages in the development of a particular cancer in an adult person, over a period of 27 years.



Which shows the processes happening between each of the stages indicated?

	stage 1 to stage 2	stage 3 to stage 4	stage 4 to stage 5	stage 5 to stage 6
A	mutation	proliferation	mutation and proliferation	mutation and proliferation
B	mutation	mutation and proliferation	proliferation	mutation and proliferation
C	mutation and proliferation	mutation and proliferation	proliferation	mutation
D	Mutation (appearance of mutated cells which look abnormal)	Mutation (appearance of mutated cells which look abnormal)	Proliferation (increase in number of abnormal cells)	mutation (appearance of mutated cells which look abnormal)

4 It has been suggested that breast cancer cells produce high levels of hydrogen peroxide. This causes connective tissue cells near the cancer cells to digest some of their mitochondria, releasing nutrients which feed the cancer cells.

Which observations made on breast cancer cells and connective tissue cells growing in tissue culture support this view?

1 Breast cancer cells grown alone produce hydrogen peroxide. Stated by the first sentence.
2 Treating breast cancer cells with hydrogen peroxide causes apoptosis. Question did not mention anything about apoptosis.
3 Connective tissue cells grown with breast cancer cells have reduced mitochondrial activity. Due to the hydrogen peroxide causing neighbouring connective tissue cells to digest their mitochondria (2nd sentence in the question).
4 Treating breast cancer cells with peroxidase increases cancer cell death. Peroxidase breaks down the hydrogen peroxide produced by cancer cells, resulting in less digestion of mitochondria in neighbouring connective tissue cells, hence less nutrients to feed the cancer cells.

A 1, 2, 3 and 4
B 1, 3 and 4 only
C 1 and 4 only
D 2 and 3 only

5 Mammalian cells growing in tissue culture divide for several generations and form thin layers on solid surfaces. Growth is inhibited by cell-cell contact (contact inhibition).

After the majority of cells have died, cancerous cells may remain as a result of changes that occurred in three stages.

Immortalization → transformation → metastasis

Descriptions of the cells in each of these stages are listed.

1 Cells can divide indefinitely and become mobile, migrating to form new colonies.
2 Cells can divide indefinitely and show contact inhibition.
3 Cells can divide indefinitely and do not show contact inhibition.

Which row correctly describes the cells at each of these three stages?

	Immortalisation	Transformation	Metastasis
A	1	2	3
B	2	1	3
C	2	3	1
D	3	2	1

Error editing:

Development of cancer is a multi-step process. Occasionally, a single mutation is sufficient to transform a normal cell into a malignant cell.

Some mutations may cause activation of telomere gene. Telomerase enzyme prevents end replication problem from occurring, hence preventing the shortening of the chromosome ends. As such, the cell can continue to divide indefinitely.

Some mutations cause cells to lose the ability to differentiate.

Some mutations cause cells to no longer exhibit anchorage dependence where the cancer cells can divide well beyond a single layer and pile up in chaotic fashion.

Some mutations cause a loss of density-dependent inhibition where the cancer cells are capable of cell division in suspension as they have developed the ability to break down substances around it to create more space to grow and divide.

The accumulation of mutations may result in the formation of malignant tumours.

Mutations can also lead to metastasis, where there is a formation of new network of blood vessels to the cancer cells. The blood vessels provide the cancer cells oxygen and nutrients for growth and to remove any waste products.

Some mutations allow for angiogenesis to occur where cancer cells are able to break loose and travel in the bloodstream and invade other tissues to form secondary tumours. At this point, the tumour is considered benign.

Answer:

Development of cancer is a multi-step process. ~~Occasionally,~~ a single mutation is not sufficient to transform a normal cell into a malignant cell.

Some mutations may cause activation of ~~telomere~~ telomerase gene. Telomerase enzyme ~~prevents end replication problem from occurring~~, (end replication problem still occurs after every round of DNA replication) elongates the telomeres using its RNA template, hence preventing the shortening of the chromosome ends. As such, the cell can continue to divide indefinitely.

Some mutations cause cells to lose the ability to differentiate.

Some mutations cause cells to no longer exhibit ~~anchorage-dependence~~ density-dependent inhibition where the cancer cells can divide well beyond a single layer and pile up in chaotic fashion.

Some mutations cause a loss of ~~density-dependent~~ anchorage-dependent inhibition where the cancer cells are capable of cell division in suspension as they have developed the ability to break down substances around it to create more space to grow and divide.

These accumulation of mutations may results in the formation of ~~malignant~~ benign tumours.

Mutations can also lead to ~~metastasis~~ angiogenesis, where there is a formation of new network of blood vessels to the cancer cells. The blood vessels provide the cancer cells oxygen and nutrients for growth and to remove any waste products.

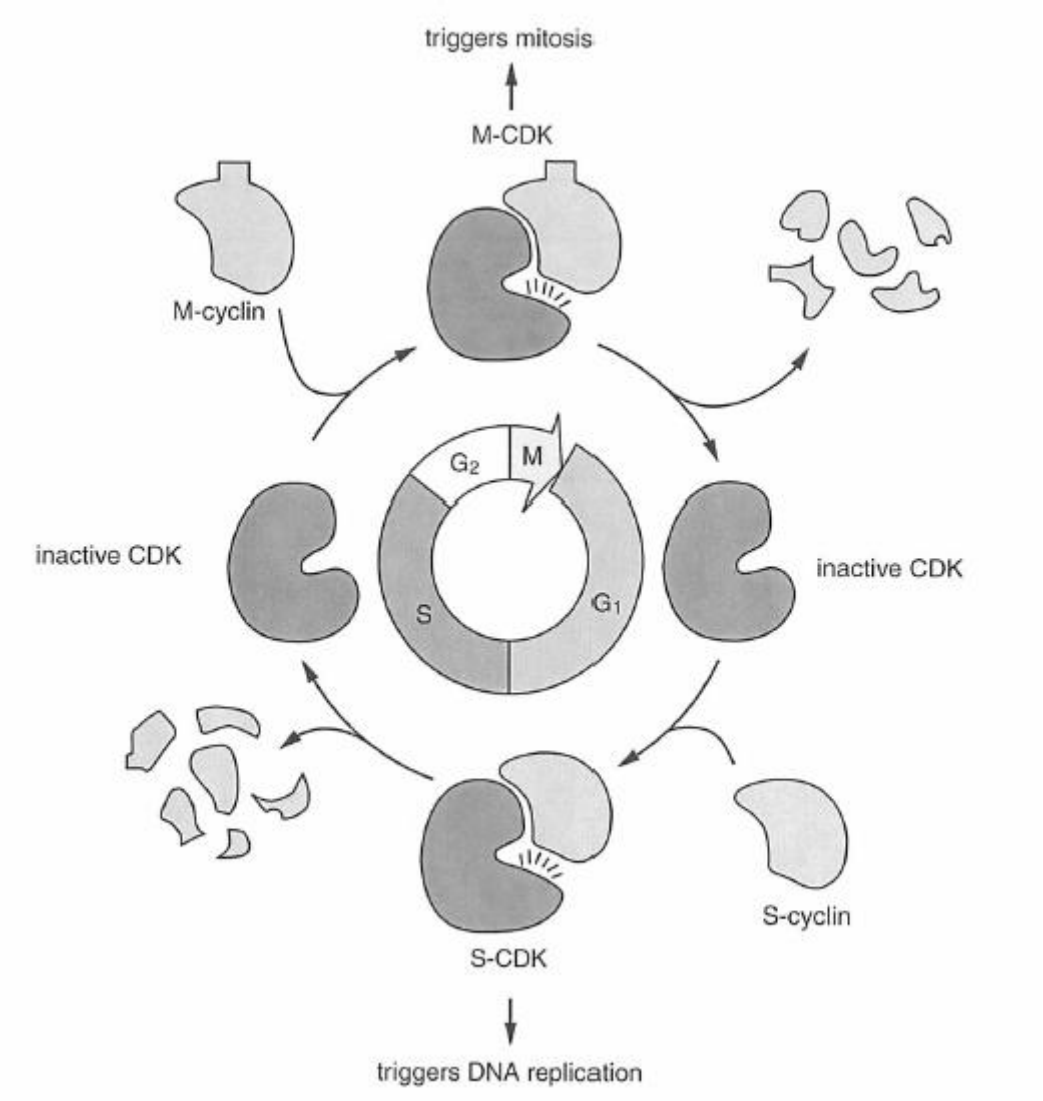
Some mutations allow for ~~angiogenesis~~ metastasis to occur where cancer cells are able to break loose and travel in the bloodstream and invade other tissues to form secondary tumours. At this point, the tumour is considered ~~benign~~ malignant.

STRUCTURED QUESTIONS
QUESTION 1 (9648 / 2013 / 2 / Q2)
In normal cells, the cell cycle is controlled at checkpoints.

In cancer, in addition to altered growth-controlling genes, many types of cancerous cells have inactivated checkpoint controls. These checkpoints involve proteins called Cyclin-Dependent-Kinases (CDKs).

CDK proteins are inactive but are activated by binding to cyclins, which are broken down after use.
CDK levels are constant whereas cyclins undergo synthesis and degradation in each cell cycle.

Fig. 2.1 shows the main stages in the cell cycle and two of these checkpoints.



(a) State what happens if a cell loses control of the cell cycle.
…….. [1]

1 It undergoes <u>uncontrolled cell division</u> and may result in cancer.

(b) With reference to Fig. 2.1, suggest how the dysregulation of checkpoints of cell division may occur.

…… [3]

1 Genes coding for M-cyclin and S-cyclin may be mutated;
resulting in production of constitutively active M-cyclins and S-cyclins / M-cyclins and S-cyclins which are resistant to degradation;

2 These cyclins bind to and activate their respective CDK proteins **continuously**;

3 The permanently activated CDK proteins allow the cells, normal or otherwise, to proceed from G2 to M phase [quoting of diag],
and from G1 to S [quoting of diag] phases of the cell cycle **without any control**;

4 This results in continuous DNA replication and mitosis and hence uncontrolled cell division.

OR

1 Genes coding for CDK may be mutated;
resulting in CDK **protein permanently binding / binding tightly** to M-cyclins and S-cyclins [quoting of diag]

2 CDK proteins activated **continuously**;

3 The permanently activated CDK proteins allow the cells, normal or otherwise, to proceed from G2 to M phase,
and from G1 to S phases of the cell cycle **without any control**;

4 This results in continuous DNA replication and mitosis and hence uncontrolled cell division.

OR

1 Genes coding for CDK may be mutated;

2 resulting in **constitutively active** CDK **protein without the need for cyclins**

3 The permanently activated CDK proteins allow the cells, normal or otherwise, to proceed from G2 to M phase,
and from G1 to S phases of the cell cycle **without any control**;

4 This results in continuous DNA replication and mitosis and hence uncontrolled cell division.

AVP → Mutation in promoter/control element of genes encoding cyclins → over expression of cyclin proteins at a rate higher than degradation

Examiner's comments: Candidates who considered the information provided in the diagram in the context of loss of control of the cell cycle were able to provide full responses. Not all considered mutations as a possible cause of changes. A significant minority of candidates described changes that would have arrested the cell cycle completely, such as cyclins being unable to bind with CDK.

(c) **(i)** Name **one** causative agent of cancer.

..... [1]

1 Ionizing radiation such as X-ray *(give at least one example)*
/ chemical carcinogens like Ethidium bromide
/ UV radiation
/ Viruses;

(d) **(ii)** Outline the development of cancer including the effects of this causative agent.

…… [3]

1 Exposure to UV (or X-rays or carcinogenic chemicals –as *according to (c)(i) answer*) can cause mutations to occur ;
2 Cells will be able to progress through the cell cycle checkpoints unchecked;
3 **Increasing cell divisions increases the chances of mutations** in other critical genes such genes pertaining to **telomerase expression, angiogenesis, density-dependence inhibition, and anchorage dependence (any 2)**
4 Accumulation of these mutations would lead to the formation of mass of cells / tumour that can become **malignant**.

[Total: 10]

QUESTION 2 (9744/2019/P3Q1b)
Curcumin is a yellow pigment found in the spice turmeric, which is used in curry powder. Curcumin also has medicinal properties.

(a) *In vitro* experiments show that curcumin decreases the proliferation of cancer cells are cultured in laboratory apparatus.

In one experiment, the mitotic cell cycle of cancer cells in culture was synchronised so that they all entered G_1 phase at the same time. The cells were then transferred to culture media containing different concentrations of curcumin. Nine hours later, the percentage of cells in each phase of interphase was recorded. None of the cells had completed the G_2 phase of interphase.

The results of this experiment are shown in Fig. 1.2.

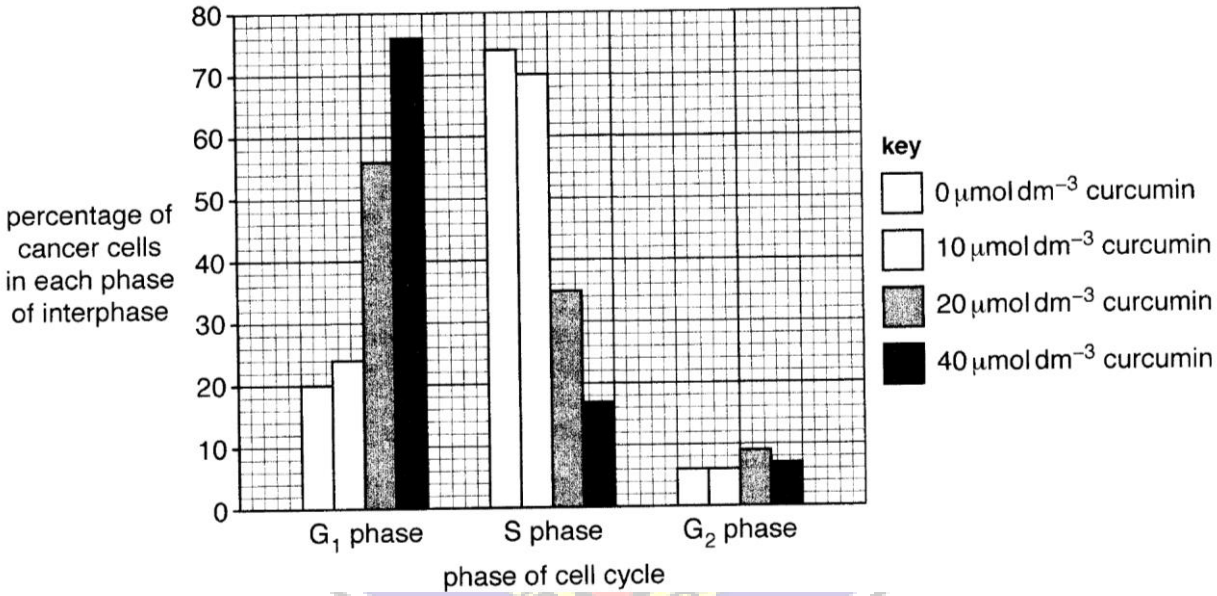


Fig. 1.2

(i) With reference to Fig. 1 .2, describe the effect of curcumin on the percentage of cancer cells in each phase of interphase nine hours after entering G_1 phase.

……..... [3]

1 Higher concentration of curcumin results in increased percentage of cancer cells substantially at G1 phase ; for example doubling the concentration of curcumin from 10 to 20 μmol dm^{-3} increased the percentage of cancer cells at G1 phase from 24 to 56% ; at 40 μmol dm^{-3} of curcumin, the percentage of cancer cells at G1 phase increases to 76% ;

2 Higher concentration of curcumin decreases the percentage of cancer cells at S phase ; for example at 40 μmol dm^{-3} curcumin, the percentage of cancer cells is decreased drastically at S phase to 17% compared to the control (0 μmol dm^{-3} curcumin) at 74% ;

3 Varying the concentration of curcumin from 10 to 40 μmol dm^{-3} has no or little impact on the percentage of cancer cells ; the percentage of cancer cells at 20 μmol dm^{-3} remained as 6%, same as the control while the percentage of cancer cells at 30 and 40 μmol dm^{-3} are at 9% and 7%, respectively ;

Examiner's comments:

Most candidates were able to use Fig. 1.2 to describe the effect of curcumin on one or two of the phases of interphase. Stronger responses separately addressed each of the three phases and compared the absence of curcumin with a high or a range of concentrations of curcumin. Better descriptions highlighted trends and meaning and did not consist of figures alone. Weaker responses did not include any judgement as to whether curcumin in a given phase makes the percentage of cancer cells higher or lower.

(ii) With reference to Fig. 1.2, suggest how curcumin affects the mitotic cell cycle and how this could help in the treatment of cancer.

…… [4]

1 [Quoting data]: When 40 µmol dm^{-3} of curcumin was added, 76% of cancer cells stayed at G1 phase, and only 17% could progress to S phase and 7% to G2 phase.

2 There is a **reduction in the number of cancer cells** progressing through **G1 checkpoint**

3 and hence reducing number of cancer cells undergoing DNA replication in S phase of interphase and G2 phase.

4 Rate of cell division is reduced, hence slows down the development of tumours.

AVP: Slows down accumulation of further mutations, e.g. genes that allow for metastasis (give at least 1 e.g.)

Examiner's comments:

*Weak responses often repeated descriptions and figures that were more relevant to **(b)(i)**. Stronger responses used the trends described in **(b)(i)** to identify the checkpoint at which curcumin halts the cell cycle, the further events that would not occur (or would occur less) and how this would affect the number of cancer cells and the development of tumours. A major misconception that appeared quite frequently was that mitosis occurs during S phase of interphase. Candidates appeared to be confusing DNA replication with nuclear division.*