LEC 15 CYTOLOGY Q:

1. **Which of the following mutations is most likely to drive the transition from a benign adenoma to a carcinoma in the colorectal cancer progression model described by Feron and Vogelstein?**

A. Mutation in kRAS oncogene
B. Mutation in the β-catenin pathway
C. Activation of the PI3K/Akt pathway
D. Loss of p53 function

2. **The overexpression of HER2 in breast cancer is primarily due to:**

A. Gene amplification, which increases the number of HER2 receptors on the cell surface
B. Loss of the p53 tumor suppressor function
C. An overproduction of EGF, which binds and activates HER2 receptors
D. A mutation in the HER2 gene resulting in a constitutively active receptor

3. **Which of the following is true about the PI3K/Akt signaling pathway in cancer?**

A. PI3K inhibits Akt to prevent cell survival.
B. Mutations in PTEN, a tumor suppressor gene, can lead to Akt hyperactivation, promoting cell survival and proliferation.
C. Akt directly inhibits the MAPK signaling cascade.
D. The pathway promotes apoptosis in response to DNA damage.

4. **What is the role of E-cadherin loss in cancer metastasis?**

A. It promotes autocrine growth stimulation by increasing receptor activation.
B. It prevents angiogenesis by inhibiting blood vessel formation.
C. It enhances integrin-mediated adhesion to the extracellular matrix.
D. It results in increased mesenchymal-like behavior and facilitates cell migration.

5. **In the context of oncogenesis, the mutation in RAS leading to a Gly12Val change results in which of the following outcomes?**

A. The mutation results in an overactive p53 pathway, leading to apoptosis.
B. RAS prevents RAF activation, blocking downstream signaling.
C. RAS remains constitutively active, continuously promoting cell division.
D. The RAS protein becomes inactive, preventing cell growth.

6. **Which of the following best describes the action of the monoclonal antibody Herceptin (trastuzumab) in the treatment of HER2-positive breast cancer?**

A. Herceptin blocks the HER2 receptor, preventing its overactivation and subsequent tumor growth.
B. Herceptin activates the HER2 receptor, promoting tumor cell apoptosis.
C. Herceptin stimulates angiogenesis, supplying the tumor with nutrients.
D. Herceptin induces DNA damage in the tumor cells, promoting cell death.

7. **Inactivation of the RB gene leads to:**

A. Increased differentiation of cancer cells into specialized tissue types.
B. Uncontrolled progression of the cell cycle from G1 to S phase.
C. Induction of apoptosis via the p53 pathway.
D. Inhibition of angiogenesis by blocking VEGF signaling.

8. **Which of the following is the most significant consequence of p53 loss or mutation in cancer cells?**

A. The loss of p53 prevents DNA damage repair and allows damaged cells to proliferate.
B. The absence of p53 promotes the differentiation of tumor cells into functional tissue.
C. The loss of p53 leads to excessive apoptosis in the tumor.
D. The mutation of p53 directly activates oncogenes like RAS and MYC.

9. **In acute promyelocytic leukemia (APL), the fusion of the PML gene with the RARα gene leads to:**

A. Enhanced migration and metastasis of leukemic cells.
B. Increased telomerase activity, promoting immortality of the cells.
C. Prevention of normal differentiation, keeping cells in a proliferating state.
D. Activation of the p53 pathway, triggering apoptosis.

10. **Helicobacter pylori, a bacterial pathogen, is implicated in the development of which of the following cancers?**

A. Gastric (stomach) cancer
B. Lung cancer

C. Colorectal cancer
D. Liver cancer

11. **The MAPK signaling pathway is often activated by mutations in which of the following proteins in cancer cells?**

A. PTEN
B. RAS
C. p53
D. E-cadherin

12. **The loss of E-cadherin expression in cancer cells contributes to which of the following features?**

A. Induction of cell cycle arrest
B. Enhanced cell migration and invasiveness
C. Increased apoptosis through p53 activation
D. Suppression of angiogenesis

13. **The BRCA1 and BRCA2 tumor suppressor genes play a critical role in which of the following processes?**

A. Inhibiting HER2 signaling in breast cancer
B. Stimulating angiogenesis in tumors
C. Activating the PI3K/Akt survival pathway
D. Repairing DNA double strand breaks through homologous recombination

14. **Which of the following best describes the role of telomerase in cancer cells?**

A. It prevents DNA damage by stabilizing the cell cycle.
B. It inhibits the activation of oncogenes like RAS and MYC.
C. It promotes apoptosis by shortening telomeres.
D. It maintains telomere length, allowing for continued cell division and tumor growth.

15. **The PI3K/Akt pathway plays a key role in regulating:**

A. The G1 to S transition in the cell cycle.
B. The survival of cancer cells by inhibiting pro-apoptotic proteins.

C. The differentiation of stem cells into specialized tissue types.
D. The induction of apoptosis in response to DNA damage.

Answers:

1. B
2. A
3. B
4. D
5. C
6. A
7. B
8. B
9. C
10. B
11. B
12. B
13. D
14. D
15. B

1. The loss of contact inhibition in cancer cells is primarily associated with:
A. Mutations in RB and p16 genes that disrupt cell cycle regulation
B. Dysregulation of E-cadherin and cell-cell adhesion
C. The overactivation of p53 tumor suppressor function
D. Increased tumor angiogenesis

2. A mutation in the RAS gene causing a Gly12Val substitution results in:
A. Deactivation of RAF, preventing activation of the downstream MAPK pathway
B. Inhibition of PI3K/Akt signaling, resulting in cell death
C. An inability to hydrolyze GTP, keeping RAS in its active form and leading to continuous signaling for cell growth
D. A decrease in the affinity of RAS for its binding partners, thereby inhibiting cell division

3. The PI3K/Akt signaling pathway is frequently activated by mutations in which of the following tumor suppressor genes?
A. RB
B. p53
C. BRCA1
D. PTEN

4. The PML/RARα fusion gene in acute promyelocytic leukemia (APL) is an example of:
A. A viral oncogene that stimulates cell proliferation
B. An epigenetic change that silences tumor suppressor gene expression

C. A genetic translocation that prevents differentiation and promotes uncontrolled proliferation
D. A tumor suppressor gene mutation leading to loss of differentiation

5. Which of the following correctly describes the mechanism of Herceptin (trastuzumab) in HER2-positive breast cancer treatment?
A. Herceptin acts as a growth factor that enhances signaling through HER2 receptors
B. Herceptin binds to HER2 receptors and induces internalization, preventing receptor signaling, and promoting apoptosis
C. Herceptin prevents HER2 expression by blocking its transcription
D. Herceptin activates p53 to induce apoptosis in tumor cells

6. E-cadherin loss in tumor cells contributes to:
A. Increased sensitivity to contact inhibition
B. Decreased cell migration and invasiveness
C. An epithelial-to-mesenchymal transition (EMT), enhancing migration and metastasis
D. Increased apoptosis through activation of the p53 pathway

7. A mutation in BRCA1 or BRCA2 can lead to:
A. Inhibition of homologous recombination repair, causing genomic instability
B. Increased DNA damage repair through base excision repair
C. Activation of the PI3K/Akt pathway, leading to enhanced cell survival
D. Decreased telomerase activity, leading to reduced cell proliferation

8. The PTEN tumor suppressor gene normally functions to:
A. Activate angiogenesis to support tumor growth
B. Inhibit the PI3K/Akt pathway by dephosphorylating PIP3, preventing cell survival signals
C. Stimulate DNA repair and prevent genomic instability
D. Activate RAS signaling to promote cell growth

9. The MAPK pathway is critical for cell proliferation. Mutations in RAS or RAF commonly lead to:
A. Reduced angiogenesis and inhibition of metastasis
B. Constitutive activation of downstream signaling, leading to uncontrolled cell growth
C. Inhibition of cell cycle progression and promotion of cell death
D. Increased differentiation of cancer cells into specialized cell types

10. Telomerase activity in cancer cells helps maintain genomic stability by:
A. Enhancing immune surveillance and detection of tumor cells
B. Promoting cell differentiation and limiting cell division
C. Extending telomeres to allow continued cell proliferation and avoid cell senescence
D. Inducing apoptosis in cells with shortened telomeres

11. The loss of p53 function in tumor cells often leads to:
A. The inability of cells to undergo apoptosis in response to DNA damage, leading to proliferation of damaged cells
B. Increased DNA repair and enhanced genomic stability

C. Decreased cellular proliferation through cell cycle arrest
D. Activation of BRCA1/BRCA2 repair mechanisms to fix DNA breaks

12. The HER2 receptor is a proto-oncogene. Its overexpression in breast cancer is linked to:
A. Gene amplification resulting in excessive activation of the MAPK and PI3K/Akt pathways
B. Inactivation of p53 and suppression of apoptosis
C. Decreased angiogenesis and blood vessel formation in tumors
D. Loss of E-cadherin, leading to increased tumor cell differentiation

13. The RB protein functions primarily to regulate:
A. Apoptosis in response to oncogene activation
B. The G1 to S phase transition of the cell cycle
C. Angiogenesis and blood supply to tumors
D. Activation of tumor suppressor genes like p53

14. Which of the following best describes the relationship between oncogenes and tumor suppressor genes?
A. Oncogenes promote cell cycle arrest, while tumor suppressor genes stimulate cell growth.
B. Both oncogenes and tumor suppressor genes act to inhibit cell growth and prevent tumor formation.
C. Oncogenes are mutations of normal genes that promote cancer by stimulating cell proliferation, while tumor suppressor genes prevent cancer by regulating cell cycle checkpoints.
D. Oncogenes and tumor suppressor genes are unrelated and function independently in cancer progression.

15. A mutation in the RAS gene that results in constitutive activation of the RAF kinase can lead to:
A. Reduced expression of cyclins and decreased cell proliferation
B. Normal cell cycle regulation and differentiation
C. The continuous activation of the MAPK signaling pathway, resulting in unregulated cell growth
D. Inhibition of MEK, blocking cell cycle progression

16. p53 is a key regulator of the cell cycle. Inactivation of p53 in cancer cells is most likely to result in:
A. Increased ability to repair DNA damage
B. Uncontrolled cell division despite the presence of DNA damage
C. Prevention of tumor metastasis by inhibiting MMPs
D. Enhanced apoptosis in response to oncogene activation

17. Cdk4/Cyclin D activity is essential for the progression of cells from G1 to S phase. Inactivation of the RB protein results in:
A. Activation of the p53 pathway, inducing apoptosis
B. Cell cycle arrest at the G1 checkpoint
C. Uncontrolled cell cycle progression, leading to cancer
D. Decreased cell cycle progression due to failure to activate Cyclin D

18. Telomerase overexpression in cancer cells allows them to:
A. Degrade extracellular matrix proteins, enabling metastasis
B. Maintain telomere length, allowing cells to avoid senescence and continue dividing indefinitely
C. Reduce the mutation rate in tumor cells by enhancing DNA repair
D. Activate the p53 pathway to trigger apoptosis in damaged cells

19. The ability of cancer cells to induce angiogenesis is primarily regulated by:
A. Inhibition of the PI3K/Akt pathway
B. VEGF (vascular endothelial growth factor) expression
C. E-cadherin signaling
D. RB protein inactivation

20. Helicobacter pylori infection contributes to gastric cancer by:
A. Increasing expression of VEGF, promoting angiogenesis in gastric tumors
B. Suppressing p53 function, allowing for cell survival despite genetic mutations
C. Increasing EGF receptor expression, stimulating cell growth
D. Inducing inflammation and DNA damage, leading to mutations in gastric cells

Answers:

1. B
2. C
3. D
4. C
5. B
6. C
7. A
8. B
9. B
10. C
11. A
12. A
13. B
14. C
15. C
16. B
17. C
18. B
19. B
20. B

1. Which of the following mutations is most likely to lead to uncontrolled activation of the Ras-Raf-MAPK pathway, promoting cancer cell proliferation?
A. A mutation in p53 that prevents cell cycle arrest
B. A G12V mutation in RAS, causing it to remain in an active GTP-bound state
C. A frame-shift mutation in RB, leading to loss of function
D. A mutation in PTEN, causing a reduction in PI3K pathway activation

2. The BRCA1 and BRCA2 genes are critical for maintaining genomic stability by:
A. Enhancing the efficiency of the MAPK pathway in cancer cells
B. Promoting repair of DNA double-strand breaks through homologous recombination
C. Inducing apoptosis in cells with damaged DNA via the p53 pathway
D. Activating telomerase to maintain telomere length in cancer cells

3. E-cadherin dysfunction in cancer cells typically leads to:
A. Increased cell adhesion and reduced tumor invasiveness
B. Loss of epithelial characteristics, triggering the epithelial-to-mesenchymal transition (EMT)
C. Activation of the PI3K/Akt pathway, promoting cell survival
D. Increased differentiation of tumor cells into specialized cell types

4. The PML/RARα fusion protein in acute promyelocytic leukemia (APL) is an example of:
A. A gain-of-function mutation that activates the RA receptor to stimulate differentiation
B. A tumor suppressor gene that prevents the proliferation of leukemic cells
C. A fusion protein that blocks normal differentiation and leads to uncontrolled cell proliferation
D. A viral oncogene that induces apoptosis and tumor regression

5. Which of the following is the primary consequence of HER2 overexpression in HER2-positive breast cancer cells?
A. Inhibition of angiogenesis, reducing tumor blood supply
B. A decrease in the activation of PI3K/Akt and MAPK signaling pathways
C. Increased sensitivity to growth factors, leading to enhanced cell proliferation
D. Decreased receptor internalization, reducing signaling transduction

6. The PI3K/Akt pathway is often upregulated in cancer through mutations in which of the following genes?
A. p53
B. BRCA2
C. PTEN
D. RB

7. The primary mechanism by which telomerase contributes to cancer cell immortality is by:
A. Preventing the activation of cyclin-dependent kinases (CDKs), inhibiting cell cycle progression
B. Stabilizing telomeres, thereby preventing senescence and allowing unlimited cell

division
C. Stimulating angiogenesis by promoting VEGF expression in tumor cells
D. Inducing DNA damage repair through homologous recombination in response to telomere shortening

8. p53 plays a key role in preventing tumorigenesis by:
A. Promoting the repair of DNA damage and triggering apoptosis in response to stress signals
B. Stimulating the cell cycle progression from G1 to S phase
C. Inactivating the PI3K/Akt pathway, inhibiting cell survival
D. Stimulating telomere elongation to enhance cancer cell proliferation

9. The PI3K/Akt signaling pathway contributes to cancer cell survival primarily by:
A. Inhibiting apoptosis through the activation of pro-apoptotic proteins
B. Increasing the transcription of genes that promote cell cycle arrest
C. Inducing the expression of anti-apoptotic proteins such as Bcl-2
D. Promoting tumor metastasis by enhancing cell migration and invasion

10. A mutation in the RAS gene that leads to continuous activation of RAF would most likely result in:
A. Loss of the p53 pathway and inability to repair DNA damage
B. Constitutive activation of the MAPK pathway, leading to enhanced cell proliferation
C. Blockage of Cyclin D activation, causing cell cycle arrest
D. Inhibition of VEGF signaling and reduced angiogenesis

11. The loss of contact inhibition in cancer cells is primarily due to:
A. Activation of the PI3K/Akt pathway, leading to cell survival
B. Mutation or loss of function in cell adhesion molecules like E-cadherin
C. Enhanced angiogenesis that facilitates cell migration
D. Inactivation of the p53 tumor suppressor gene, allowing uncontrolled growth

12. In hereditary breast cancer, mutations in BRCA1 or BRCA2 lead to:
A. Decreased MAPK pathway activation, preventing tumor growth
B. A defect in DNA double-strand break repair, increasing genomic instability
C. Activation of telomerase, promoting cell immortality
D. Reduced sensitivity to DNA damage, allowing the proliferation of damaged cells

13. p53 mutations in cancer cells result in:
A. Inhibition of RB phosphorylation and G1 arrest
B. The promotion of apoptosis in response to DNA damage
C. The prevention of DNA repair, leading to further mutations
D. The stimulation of angiogenesis through the activation of VEGF

14. The HER2/neu receptor in breast cancer can lead to cancer development primarily through:
A. Reduced cell proliferation and differentiation due to decreased MAPK signaling
B. Increased sensitivity to EGF, leading to the overactivation of the PI3K/Akt and MAPK pathways

C. Inhibition of apoptosis via Bcl-2 and p53 signaling
D. Suppression of angiogenesis and restriction of blood supply to the tumor

15. The RA receptor is an important target in acute promyelocytic leukemia (APL). The PML/RARα fusion gene prevents normal differentiation by:
A. Activating the expression of genes that promote cell differentiation
B. Blocking the expression of RA-responsive genes involved in differentiation
C. Enhancing apoptosis in leukemic cells
D. Activating the MAPK pathway, leading to cell growth

16. A key feature of cancer stem cells that makes them resistant to treatment is:
A. Their ability to maintain E-cadherin expression, preventing metastasis
B. Their ability to evade apoptosis through dysregulation of p53
C. Their enhanced expression of telomerase, preventing senescence
D. Their dependence on angiogenesis for tumor growth

17. PTEN functions as a tumor suppressor by:
A. Activating MAPK signaling to promote cell growth
B. Dephosphorylating PIP3, thereby preventing activation of the PI3K/Akt pathway
C. Inducing apoptosis via p53 and Bcl-2 regulation
D. Stimulating DNA repair through homologous recombination

18. Angiogenesis in tumors is often driven by the upregulation of which of the following factors?
A. VEGF (Vascular Endothelial Growth Factor)
B. p53
C. RB
D. p16INK4a

19. The epithelial-to-mesenchymal transition (EMT) observed in cancer cells is a process that:
A. Inhibits cancer cell migration and invasion
B. Leads to increased differentiation and reduced metastasis
C. Involves the loss of epithelial characteristics and increased migration, contributing to metastasis
D. Enhances the differentiation of tumor cells into specialized, non-proliferative cell types

20. Mutations in RAS and RAF commonly activate which of the following signaling cascades, contributing to tumorigenesis?
A. JAK-STAT pathway
B. PI3K/Akt pathway
C. Wnt/β-catenin pathway
D. MAPK/ERK pathway

Answers:

1. B

2. B
3. B
4. C
5. C
6. C
7. B
8. A
9. C
10. B
11. B
12. B
13. C
14. B
15. B
16. C
17. B
18. A
19. C
20. D

USMLE STEP 1:

1. Oncogene Activation and Signal Transduction

Question 1: A 50-year-old man with colorectal cancer undergoes genetic testing that reveals a mutation in the **kRAS** gene. This mutation results in a constitutively active form of kRAS. Which of the following signaling pathways is most likely to be hyperactivated in this patient?

A) JAK-STAT pathway
B) MAPK (Ras-Raf-MEK-ERK) pathway
C) PI3K-AKT pathway
D) Wnt-β-catenin pathway
E) Notch signaling pathway

Answer: B

Explanation: The **kRAS** gene encodes a GTPase that is a central player in the **MAPK signaling pathway**, which regulates cell proliferation, survival, and differentiation. A constitutively active kRAS leads to persistent activation of this pathway, driving uncontrolled cell growth and contributing to cancer progression.

---

2. Tumor Suppressor Gene Function

Question 2: A 48-year-old woman with a family history of ovarian cancer undergoes genetic testing and is found to carry a mutation in the **BRCA1** gene. Which of the following mechanisms is most likely impaired in this patient, leading to an increased risk of cancer?

A) DNA repair of double-strand breaks
B) Activation of the p53 pathway to induce apoptosis
C) Inhibition of telomerase activity
D) Suppression of angiogenesis
E) Activation of the Rb pathway to arrest the cell cycle

Answer: A

Explanation: **BRCA1** is involved in the repair of **DNA double-strand breaks** through homologous recombination. Mutations in BRCA1 lead to defective DNA repair, resulting in genomic instability and an increased risk of breast and ovarian cancers.

---

3. Molecular Basis of Tumor Angiogenesis

Question 3: A 45-year-old male patient with a history of prostate cancer develops an aggressive tumor that is characterized by a high rate of angiogenesis. The tumor cells secrete large amounts of **VEGF** (vascular endothelial growth factor). Which of the following is the most likely consequence of this VEGF secretion?

A) Inhibition of the MAPK pathway
B) Increased cell-cell adhesion via integrin signaling
C) Formation of new blood vessels to supply the tumor with oxygen and nutrients
D) Inactivation of p53, leading to resistance to apoptosis
E) Activation of telomerase to prevent telomere shortening

Answer: C

Explanation: **VEGF** is a key driver of **angiogenesis**, the process of forming new blood vessels. In tumors, VEGF secretion enables the tumor to form new vessels, which supply oxygen and nutrients necessary for tumor growth and progression.

---

4. Role of Oncogenes in Cancer

Question 4: A 50-year-old man presents with gastric cancer and is found to have a **c-MYC** oncogene amplification. Which of the following is the most likely consequence of **c-MYC** activation in this patient's tumor cells?

A) Inhibition of the cyclin-CDK complex
B) Upregulation of pro-apoptotic proteins such as Bax
C) Activation of the cell cycle and promotion of cell proliferation
D) Induction of senescence through the p16INK4A pathway
E) Stabilization of the retinoblastoma protein (Rb)

Answer: C

Explanation: **c-MYC** is a transcription factor that promotes the expression of genes involved in cell cycle progression, particularly those that activate the **G1 to S phase transition**. Its overexpression leads to uncontrolled cell division and contributes to tumorigenesis.

---

5. Viral Oncogenesis

Question 5: A 32-year-old woman presents with an abnormal Pap smear, and HPV testing reveals a high-risk strain. She is diagnosed with cervical cancer. Which of the following viral proteins is most responsible for the oncogenic potential of HPV in this patient?

A) E1
B) E2
C) E6
D) E7
E) E4

Answer: C

Explanation: The **E6** protein of high-risk **HPV** strains promotes the degradation of **p53**, a key tumor suppressor protein that regulates the cell cycle and apoptosis. This leads to loss of cell cycle checkpoints and resistance to apoptosis, contributing to oncogenesis.

---

6. Tumor Suppressor Gene Mutations in Cancer

Question 6: A 50-year-old woman with breast cancer undergoes genetic testing and is found to have a mutation in the **p53** tumor suppressor gene. This mutation is most likely to lead to which of the following?

A) Inhibition of angiogenesis
B) Increased telomerase activity
C) Loss of cell cycle arrest in response to DNA damage
D) Decreased cell proliferation
E) Increased apoptosis in response to DNA damage

Answer: C

Explanation: **p53** is a tumor suppressor that activates cell cycle arrest (via **p21**) in response to DNA damage, allowing time for repair or induction of apoptosis if repair is not possible. Mutations in **p53** prevent this response, contributing to unchecked cell division and cancer progression.

---

7. Genomic Instability and Cancer Risk

Question 7: A patient with a family history of colon cancer undergoes genetic testing and is found to have a mutation in the **MSH2** gene. This gene is involved in DNA mismatch repair. Which of the following is the most likely outcome of this mutation?

A) Increased telomerase activity and extended cellular lifespan
B) Accumulation of mutations due to impaired DNA repair
C) Activation of tumor suppressor genes such as p16INK4A
D) Inhibition of angiogenesis through VEGF suppression
E) Decreased cell proliferation due to cell cycle arrest

Answer: B

Explanation: **MSH2** is involved in the **mismatch repair** of DNA. Mutations in this gene lead to defective DNA repair and the accumulation of mutations in the genome, a hallmark of **microsatellite instability** seen in cancers such as colon cancer, particularly in the **Lynch syndrome**.

---

8. Cancer Metastasis and Molecular Mechanisms

Question 8: A 65-year-old man with lung cancer presents with multiple bone lesions. Histologic examination reveals the presence of malignant cells that exhibit increased expression of **MMPs** (matrix metalloproteinases). What is the most likely role of MMPs in this patient's cancer?

A) Inhibition of apoptosis and increased survival
B) Promotion of tumor angiogenesis
C) Facilitation of tumor cell migration through the extracellular matrix
D) Activation of tumor suppressor genes to prevent metastasis
E) Prevention of telomere shortening in cancer cells

Answer: C

Explanation: **Matrix metalloproteinases (MMPs)** are enzymes that degrade extracellular matrix components, facilitating **tumor cell migration** and invasion of surrounding tissues, an essential step in **metastasis**. They play a key role in the ability of cancer cells to spread to distant organs.

---

9. Cell Cycle Regulation in Cancer

Question 9: A 42-year-old woman with breast cancer is found to have an overexpression of **Cyclin D1**. Which of the following is the most likely consequence of this overexpression in her cancer cells?

A) Increased activation of the p53 pathway leading to cell cycle arrest
B) Uncontrolled progression of the cell cycle through the G1 phase
C) Inhibition of cyclin-dependent kinases
D) Increased levels of the p16INK4A inhibitor
E) Decreased levels of the retinoblastoma protein (Rb)

Answer: B

Explanation: **Cyclin D1** binds to and activates **CDK4**, leading to the phosphorylation and inactivation of the **retinoblastoma (Rb)** protein. This allows the cell to progress from **G1 to S phase**, promoting cell proliferation and contributing to cancer.

---

10. Cancer and Epigenetic Changes

Question 10: A patient with a history of smoking is diagnosed with lung cancer. Research shows that his tumor cells have undergone **hypermethylation** of the **p16INK4A** tumor suppressor gene promoter. Which of the following is the most likely effect of this epigenetic change?

A) Increased transcription of p16INK4A and cell cycle arrest
B) Decreased expression of cyclin D1 and inhibition of CDK4
C) Activation of telomerase to prevent telomere shortening
D) Decreased expression of p16INK4A, leading to loss of cell cycle control
E) Increased expression of pro-apoptotic proteins such as Bax

Answer: D

Explanation: **Hypermethylation** of the **p16INK4A** gene promoter results in **silencing** of its expression, leading to loss of cell cycle control. p16INK4A normally inhibits the **CDK4-cyclin D** complex, preventing the cell from progressing through the G1 phase, but its loss contributes to uncontrolled cell proliferation.