

1-A 38-year-old woman has abdominal distention that has been worsening for the past 6 weeks. An abdominal CT scan shows bowel obstruction caused by a 6-cm mass in the jejunum. At laparotomy, a portion of the small bowel is resected. Flow cytometric analysis of a portion of the tumor shows a clonal population of B lymphocytes with high Sphase. Translocation with activation of which of the following nuclear oncogenes is most likely to be present in this tumor?

- A- *APC*
- B -*EGF*
- C -*MYC*
- D -*p53*
- E -*RAS*

2-A 70-year-old woman reported a 4-month history of a 4-kg weight loss and increasing generalized icterus. On physical examination, she has mi epigastric tenderness on palpation. An abdominal CT scan shows a 5-cm mass in the head of the pancreas. Fine-needle aspiration of the mass is performed. On biochemical analysis, the neoplastic cells show continued activation of cytoplasmic kinases. Which of the following genes is most likely to be involved in this process?

- A *APC*
- B *MYC*
- C *p53*
- D *RAS*
- E *RET*
- F *sis*

3-A 30-year-old man has a pheochromocytoma of the left adrenal gland; a sibling had a cerebellar hemangioblastoma. He undergoes adrenalectomy, and on microscopic examination there is extensive vascularity of the neoplasm. Mutational analysis of the neoplastic cells shows that both allelic copies of a gene have been lost, so that a protein that binds to hypoxia-inducible factor 1-alpha is no longer ubiquitinated, but instead translocate to the nucleus and activates transcription of *VEGF*. Which of the following genes is most likely

mutated in this man?

A- *APC*

B- *BCL2*

C- *EGF*

D- *HER2*

E- *VHL*

4- A 35-year-old man living in a southern region of Africa presents with increasing abdominal pain and jaundice. He has worked as a farmer for many years, and sometimes his grain has become moldy. Physical examination reveals a large mass involving the right side of his liver, and a biopsy specimen from this mass confirms the diagnosis of liver cancer (hepatocellular carcinoma). Which of the following substances is most closely associated with the pathogenesis of this tumor?

- a. Aflatoxin B1
- b. Direct-acting alkylating agents
- c. Vinyl chloride
- d. Azo dyes
- e. β -naphthylamine

5- A 59-year-old man is found to have a 3.5-cm mass in the right upper lobe of his lung. A biopsy of this mass is diagnosed as a moderately differentiated squamous cell carcinoma. Workup reveals that no bone metastases are present, but laboratory examination reveals that the man's serum calcium levels are 11.5 mg/dL. This patient's paraneoplastic syndrome is most likely the result of the ectopic production of which of the following substances?

- a. Parathyroid hormone
- b. Parathyroid hormone-related peptide
- c. Calcitonin
- d. Calcitonin-related peptide

e. Erythropoietin

6- Which one of the listed statements best describes the mechanism through which Fas (CD95) initiates apoptosis?

a. BCL2 product blocks bax channels

b. Cytochrome c activates Apaf-1

c. FADD stimulates caspase 8

d. TNF inhibits IKB

e. TRADD stimulates FADD

7-A patient presents with a large wound to his right forearm that is the result of a chain saw accident. You treat his wound appropriately and follow him in your surgery clinic at routine intervals. Initially his wound is filled with granulation tissue, which is composed of proliferating fibroblasts and proliferating new blood vessels (angiogenesis). Which of the following substances is thought to be the most important growth factor involved in angiogenesis?

a. Epidermal growth factor (EGF)

b. Platelet-derived growth factor (PDGF)

c. Transforming growth factor-alpha (TGF- α)

d. Transforming growth factor-beta (TGF- β)

e. Vascular endothelial growth factor (VEGF)

8-A 54-year-old woman notes a lump in her right breast. Physical examination shows a 2-cm mass fixed to the underlying tissues beneath the areola and three firm, nontender, lymph nodes palpable in the right axilla. There is no family history of cancer. An excisional breast biopsy is performed, and microscopic examination shows the findings in the figure. Over the next 6 months, additional lymph nodes become enlarged, and CT scans show nodules in the lung, liver, and brain. Which of the following molecular abnormalities is most likely to be found in her carcinoma cells?

- A -Amplification of the ERBB2 (HER2) gene
- B -Deletion of one RB gene copy
- C -Fusion of BCR and C-ABL genes
- D -Inactivation of one BRCA1 gene copy
- E -Mutation of one p53 gene copy

9-A 34-year-old sexually active woman undergoes a routine physical examination. There are no abnormal findings. A Pap smear is obtained as part of the pelvic examination. Cytologically, the cells obtained on the smear from the cervix show severe epithelial dysplasia (high-grade squamous intraepithelial lesion). Which of the following therapeutic options is most appropriate for this woman?

- A -Antibiotic therapy
- B- Excision
- C -Ovarian removal
- D -Screening of family members
- E -Watchful waiting

10-A 61-year-old woman has noted a feeling of pelvic heaviness for the past 6 months. On physical examination, there is a palpable nontender lower abdominal mass. An abdominal ultrasound scan shows a 12-cm solid mass in the uterine wall. A total abdominal hysterectomy is performed. The mass has the microscopic appearance of a well-differentiated leiomyosarcoma. One year later, a chest radiograph shows a 4-cm nodule in her right lower lung. Cytologic analysis of a fine-needle biopsy specimen of the nodule shows a poorly differentiated sarcoma. The patient's medical history indicates that she has smoked cigarettes most of her adult life. Which of the following mechanisms best explains these findings?

- A -Continued cigarette smoking by the patient
- B -Development of a second primary neoplasm
- C -Inheritance of a defective RB gene
- D -Immunodeficiency with HIV infection
- E - Metastasis from an aggressive tumor subclone

11-A 3-year-old child has exhibited difficulty with vision in her right eye. On physical examination, there is leukocoria of the right eye, consistent with a mass in the posterior chamber. MR imaging shows a mass that nearly fills the globe. The child undergoes enucleation of the right eye. Molecular analysis of the neoplastic cells indicates absence of both copies of a gene that contributes to control of the cell cycle. Which of the following genes has most likely undergone mutation in this neoplasm?

- A -BCR-ABL
- B -BCL2
- C -RB
- D -K-RAS
- E -NF1
- F -p53

12-A 76-year-old man has experienced abdominal pain for the past year. On physical examination, there is an epigastric mass. An abdominal CT scan shows a 10-cm mass in the body of the pancreas. A fine-needle biopsy specimen of this mass shows a moderately differentiated adenocarcinoma. Mutational analysis of the carcinoma cells shows inactivation of cyclin dependent kinase inhibitor with loss of growth-suppression. Regulatory pathways controlled by which of the following genes are most likely altered in this man's carcinoma?

A- BCL2

B- β -Catenin

C- MYC

D- p53

E-TGF- β

13-A 55-year-old man has had hemoptysis and worsening cough for the past month. On physical examination, wheezes are auscultated over the right lung posteriorly. A chest radiograph shows a 6-cm right perihilar mass. A fine-needle aspiration biopsy is performed and yields cells with the microscopic appearance of non-small cell bronchogenic carcinoma. Molecular analysis of the neoplastic cells shows a p53 gene mutation. Which of the following mechanisms has most likely produced the neoplastic transformation?

A- Inability to hydrolyze GTP

B- Growth factor receptor activation

C -Loss of cell cycle arrest

D -Microsatellite instability

E- Transcriptional activation

14-A 26-year-old man with a family history of colon carcinoma undergoes a surveillance colonoscopy. It reveals hundreds of polyps in the colon, and two focal 0.5-cm ulcerated areas. A biopsy specimen from an ulcer reveals irregularly shaped glands that have penetrated the muscular layer. Which of the following molecular events is believed to occur very early in the evolution of his colonic disease process?

- A-Activation of the WNT signaling pathway
- B -Inability to hydrolyze GTP-bound RAS
- C-Loss of heterozygosity affecting the p53 gene
- D-Mutations in mismatch repair genes.
- E-Translocation of BCL2 from mitochondria to cytoplasm

15-A 63-year-old man has a cough with hemoptysis for 10 days. He has a 65 pack-year history of smoking. A chest CT scan shows a 5-cm right hilar mass. Bronchoscopy is performed, and lung biopsy specimens show small cell anaplastic lung carcinoma. His family history shows three first-degree maternal relatives who developed leukemia, sarcoma, and carcinoma before age 40 years. Which of the following gene products is most likely to have been altered by mutation to produce these findings?

- A- APC (tumor suppressor)
- B- BCL2 (anti-apoptosis)
- C -K-RAS (GTP binding)
- D- NF1 (GTPase activation)
- E -p53 (DNA damage response)

16-A 53-year-old man diagnosed with oral cancer and treated with radiation and chemotherapy 1 year ago now has a positron emission tomography (PET) scan of his neck that shows a single focus of increased uptake. This focus is resected and microscopic examination shows that it is a metastasis. Molecular analysis of this cancer shows p53, PTEN, and c-MYC gene mutations. Which of the following metabolic pathways is most likely up-regulated to promote his cancer cell survival and proliferation?

- A- Aerobic glycolysis
- B -Gluconeogenesis
- C -Hexose monophosphate shunt
- D -Oxidative phosphorylation
- E- Purine degradation

17-A 40-year-old man notices an increasing number of lumps in his groin and armpit over the past 5 months. On physical examination, he has generalized nontender lymph node enlargement and hepatosplenomegaly. An inguinal lymph node biopsy specimen shows a malignant tumor of small, well-differentiated lymphoid cells. Immunostaining of the tumor cells with antibody to BCL2 is positive in the lymphocytic cell nuclei. Which of the following mechanisms has most likely produced this lymphoid neoplasm?

- A- Diminished apoptosis
- B- Gene amplifications
- C- Increased tyrosine kinase activity
- D- Loss of cell cycle inhibition
- E- Reduced DNA repair

18-In an experiment, cells from human malignant neoplasms explanted into tissue culture medium continue to replicate. This allows development of “immortal” tumor cell lines that are extremely useful for the study of tumor biology and responses to therapeutic modalities. Activation of which of the following molecular components is most likely to endow these tumor cells with limitless replicative ability in vivo and in vitro?

- A- Hypoxia-induced factor 1
- B- BCL2 gene
- C- Cyclin-dependent kinase gene methylation
- D- DNA replication repair
- E- Telomerase

19-A 60-year-old man has noted a nodule in his neck that has increased rapidly in size over the past 2 months. On physical examination, there is a firm, nontender, 10-cm mass in the left lateral posterior neck that appears to be fused cervical lymph nodes. Hepatosplenomegaly is noted. A head CT scan reveals a mass in the Waldeyer ring near the pharynx. A biopsy of the neck mass is performed, and on microscopic examination shows abnormal lymphoid cells with many mitotic figures and many apoptotic nuclei. He is treated with a cocktail of cell cycle–acting chemotherapeutic agents. The cervical and oral masses shrink dramatically over the next month. Based on his history and response to treatment, the tumor cells are most likely to have which of the following features?

- A- Diminished vascularity
- B- Evolution of polyclonality
- C- High growth fraction
- D- Limited capacity to metastasize
- E -Strong expression of tumor antigens

20-A 48-year-old woman notices a lump in her left breast. On physical examination she has a firm, nonmovable, 2-cm mass in the upper outer quadrant of the left breast. There are enlarged, firm, nontender lymph nodes in the left axilla. A fine-needle aspiration biopsy is performed, and the cells present are consistent with carcinoma. A lumpectomy with axillary lymph node dissection is performed, and carcinoma is present in two of eight axillary nodes. Reduced expression of which of the following molecules by the tumor cells is most likely responsible for the lymph node metastases?

A- Estrogen receptors

B- ERBB2 (HER-2)

C- E-cadherin

D- Progesterone receptors

E- Tyrosine kinases

21-In a clinical trial, patients diagnosed with malignant melanoma are treated by infusion of autologous CD8+ T cells grown in vitro. These CD8+ T cells are known to kill melanoma cells, but not normal cells. Which of the following target antigens in the tumor cells are most likely recognized by these CD8+ T cells?

A -Class I MHC molecules with a melanoma cell peptide

B -Class I MHC molecules with a peptide from normal melanocytes and melanoma cells

C- Class I MHC molecules plus a peptide derived from carcinoembryonic antigen

D -Class II MHC molecules with a melanoma cell peptide

E -Class II MHC molecules with a peptide from normal melanocytes and

melanoma cells F Class II MHC molecules with laminin receptors on melanoma cells

22-An experiment involving carcinoma cells grown in culture studies the antitumor surveillance effects of the innate immune system. These carcinoma cells fail to express MHC class I antigens. It is observed, however, that carcinoma cells are lysed when an immune cell that has been activated by IL-2 is added to the culture. Which of the following immune cells is most likely to function in this manner?

A- CD4+ lymphocyte

B- CD8+ lymphocyte

C- Macrophage

D- Neutrophil

E- NK cell

23-A 33-year-old man has experienced occasional headaches for the past 3 months. He suddenly has a generalized seizure. CT scan of the head shows a periventricular 3-cm mass in the region of the right thalamus. A stereotactic biopsy of the mass yields large lymphoid cells positive for B cell markers. Which of the following underlying diseases is most likely to be found in this patient?

A- Diabetes mellitus

B- HIV infection

C- Hypertension

D- Multiple sclerosis

E- Tuberculosis

24-An investigational study reviews cells harvested from patients 30 to 50 years of age who had right-sided colon cancer with **multiple polyps** present. These patients typically develop multiple malignant lesions of the colon during middle age. Molecular analysis of the cells from the lesions shows changes in hPMS1, hPMS2, and hMLH1 genes. Which of the following principles of carcinogenesis is best illustrated by this study?

- A- Carcinogenesis is a multistep process
- B- Inability to repair DNA is carcinogenic
- C- Many oncogenes are activated by translocations
- D- Tumor initiators are mutagenic
- E- Tumor promoters induce proliferation

25-A 12-year-old girl and a 14-year-old boy have developed skin nodules in predominantly sun-exposed areas of their skin over the past 5 years, but their six siblings have not. On physical examination, both children are of appropriate height and weight. The skin lesions are 1- to 3-cm maculopapular nodules that are erythematous to brown-colored and have areas of ulceration. Microscopic analysis of biopsy specimens of the skin lesions shows squamous cell carcinoma. The children have no history of recurrent infections, and their parents and other relatives are unaffected. Which of the following mechanisms is most likely to produce neoplasia in these children?

- A- Inherited mutation of the p53 gene
- B- Chromosomal translocation
- C- Failure of nucleotide excision repair of DNA
- D- Ingestion of food contaminated with *Aspergillus flavus*
- E- Infection with human papillomavirus

26-A 26-year-old woman has a lump in her left breast. On physical examination, she has an irregular, firm, 2-cm mass in the upper inner quadrant of the breast. No axillary adenopathy is noted. A fine-needle aspirate of the mass shows anaplastic ductal cells. The patient's 30-year-old sister was recently diagnosed with ovarian cancer, and 3 years ago her maternal aunt was diagnosed with ductal carcinoma of the breast and had a mastectomy. Mutation involving which of the following genes is most likely present in this family?

- A- BCL2 (anti-apoptosis gene)
- B- BRCA1 (DNA repair gene)
- D- ERBB2 (growth factor receptor gene)
- E- HST1 (fibroblast growth factor gene)
- F- IL2 (growth factor gene)

27-In a study of patients with non-Hodgkin B cell lymphoma, a nuclear gene is found to be actively transcribed to mRNA and is transported into the cell cytoplasm. A protein is translated from this mRNA, with up-regulation of BCL2. In a control group without lymphoma, translation of the mRNA does not occur. How is the silencing of this active gene's mRNA most likely to occur?

- A- Absence of tRNA
- B- Binding to miRNA
- C- Methylation of DNA
- D- Mutation of mRNA
- E Up-regulation of mtDNA

28-A study of patients treated with chemotherapy protocols for cancer shows that 10% of them subsequently develop a second cancer, a much higher incidence compared with a control group not receiving chemotherapy. These chemotherapy protocols included the alkylating agent cyclophosphamide. What is the most likely mechanism by which this agent causes carcinogenesis in these treated cancer patients?

- A- Activation of protein kinase C
- B- Activation of endogenous viruses
- C- Blockage of TGF- β pathways
- D- Direct DNA damage
- E Inhibition of DNA repair
- F- Inhibition of telomerase

29-A 33-year-old woman with multiple sexual partners has had vaginal bleeding and discharge for the past 5 days. On physical examination, she is afebrile. Pelvic examination shows an ulcerated lesion arising from the squamocolumnar junction of the uterine cervix. A cervical biopsy is performed and microscopic examination reveals an invasive tumor containing areas of squamous epithelium, with pearls of keratin. In situ hybridization shows the presence of human papillomavirus type 16 (HPV-16) DNA within the tumor cells. Which of the following molecular abnormalities in this tumor is most likely related to infection with HPV-16?

- A -Functional inactivation of the RB protein
- B -Increased expression of epidermal growth factor receptor
- C -Epigenetic silencing of the RB gene
- D -Inability to repair DNA damage
- E -Trapping of the RAS protein in a GTP-bound state

30- 40-year-old man has a history of intravenous drug use. Physical examination shows needle tracks in his left antecubital fossa. He has mild scleral icterus. Serologic studies for HBsAg and anti-HCV are positive. He develops hepatocellular carcinoma 15 years later. Which of the following viral characteristics best explains why this patient developed hepatocellular carcinoma?

- A- Viral integration in the vicinity of proto-oncogenes
- B- Viral capture of proto-oncogenes from host cellular DNA
- C- Viral inflammatory changes with genomic damage
- D- Viral inactivation of RB and p53 gene expression
- E- Viral infection of inflammatory cells with host immunosuppression

31-A 61-year-old man with a history of chronic viral hepatitis has noted a 6-kg weight loss over the past 5 months. Physical examination shows no masses or palpable lymphadenopathy. An abdominal CT scan shows a nodular liver with a 10-cm mass in the right lobe. A stool guaiac test result is negative. An elevation in which of the following laboratory tests is most likely to be present in this man?

- A- Alpha-fetoprotein
- B -RB
- C- Calcitonin
- D- P53
- E- Immunoglobulin M

32-A clinical study involves patients diagnosed with carcinoma whose tumor stage is T4N1M1. The patients' survival rate 5 years from the time of diagnosis is less than 50%, regardless of therapy. Which of the following clinical findings is most likely to be characteristic of this group of patients?

- A- Cachexia
- B- Cardiac murmur

C- Icterus

D- Loss of sensation

E- Splenomegaly

F- Tympany

***just keep in mind that cachexia is characteristic for cancers with poor prognosis

33-A 76-year-old woman has reported a change in the caliber of her stools during the past month. On physical examination, there are no abnormal findings, but a stool sample is positive for occult blood. A colonoscopy is performed and a constricting mass involving the lower sigmoid colon is found. She undergoes a partial colectomy. Which of the following techniques used during surgery can best aid the surgeon in determining whether the resection is adequate to reduce the probability of a recurrence?

A- Electron microscopy

B- Fine-needle aspiration

C- Flow cytometry

D- Frozen section

E- Radiologic imaging

F- Serum carcinoembryonic antigen assay

Answers

1-C

2-D

3-E

4-A

5-B

6-C

7-E

8-A

9-A

10-E

11-C

12-E

13-C

14-A

15-E

16-A

17-A

18-E

19-C

20-C

21-A

22-E

23-B

24-B

25-C

26-B

27-B

28-D

29-A

30-C

31-A

32-A

33-D

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