

**JMD CME Program in Molecular Diagnostics 2006**  
Association for Molecular Pathology *and the*  
American Society for Investigative Pathology  
*The Journal of Molecular Diagnostics*  
**Volume 8, No. 1 (February 2006)**  
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Mark E. Sobel, MD, PhD, Director of Journal CME Programs

**CME Questions # 1-10**

**1. Hypermethylation of CpG islands in gene promoter regions is an important mechanism of gene inactivation in cancer. Based on the referenced article, concerning pathogenesis of colorectal cancer and hypermethylation of the MGMT and hMLH1 genes, select the ONE statement that is NOT true: [See J Mol Diagn 2006 8: 68-75]**

- a. An inverse relationship between hMLH1 and MGMT promoter hypermethylation was observed, which may reflect a positive selective pressure for retention of microsatellite repair function in an MGMT-deficient background.
- b. Tumors displaying hMLH1 promoter hypermethylation were more prevalent than those displaying MGMT promoter hypermethylation and were more likely to exhibit a low phenotype of microsatellite instability.
- c. Tumors displaying hMLH1 promoter hypermethylation had significantly absent expression of hMLH1, were right sided poorly differentiated tumors, and had lower levels of nodal metastasis.
- d. Those tumors displaying hypermethylation of MGMT or hMLH1 had a high percentage of absent or low expression of MGMT or hMLH1 protein, respectively.

**2. Cystic fibrosis is caused by mutations in the cystic fibrosis transmembrane conductance regulator (CFTR) gene. Based on the referenced article reporting on a homozygous 3120G>A mutation in CFTR, select the ONE statement that is NOT true: [See J Mol Diagn 2006 8: 137-140]**

- a. 3120G>A is a rare mutation that has presented with pancreatic insufficiency, mild pulmonary symptoms, and abnormal sweat chloride.
- b. Uniparental disomy for chromosome 7 may be a possible mechanism for the apparent homozygosity of the 3120G>A CFTR mutation.
- c. The 3120G>A mutation and its consistent correlation with obvious cystic fibrosis symptoms serves to discount concern associated with genotype/phenotype correlations.
- d. In clinical follow-up, pulmonary function tests were normal, clinical features of malabsorption were absent, and the patient exhibited an elevated sweat chloride of 77 mmol/L.

**3. Ulcerative colitis (UC) and Crohn's Disease (CD) are common inflammatory bowel diseases producing intestinal inflammation and tissue damage. Based on the referenced article reporting on molecular classification of UC and CD patients and their peripheral blood mononuclear cells (PBMCs), select the ONE statement that is NOT true: [See J Mol Diagn 2006 8: 51-61] \***

- a. PBMCs can serve as a surrogate tissue for the evaluation of inflammatory bowel disease as a biomarker of disease status or severity.
- b. The PBMC transcriptome can accurately reflect the global inflammatory response associated with inflammatory bowel disease, but does not distinguish between CD and UC.
- c. Transcriptome differences in PBMCs of CD and UC patients are not due to differential cellular composition since PBMC compositions in both diseases appear similar.
- d. Transcripts involved in prostaglandin synthesis are components of the PBMC profile associated with CD.

**4. Based on the referenced article reporting on transcriptional profiles of PBMCs in UC and CD patients, select the ONE statement that is NOT true: [See J Mol Diagn 2006 8: 51-61] \***

- a. UC-specific transcripts in PBMCs are dominated by immunoglobulin coding sequences.
- b. The evident upregulation of several cytokines in the PBMCs associated with CD may be related to CD-specific effects on prostaglandin synthesis.
- c. PBMC gene signatures can accurately discriminate UC from CD patient samples.
- d. The PBMC gene signatures are specific for UC and CD and distinguish these disorders from other forms of colitis and inflammatory based diseases.

**5. Circulating tumor cells can be identified in the blood of patients with solid tumors using molecular methods. Based on the referenced article reporting on molecular methods for detection of cytokeratin 20 (CK20), select the ONE statement that is NOT true: [See J Mol Diagn 2006 8: 105-112]**

- a. The association between *CK20* cell-equivalents and metastasis was statistically significant for breast and colorectal cancer patients.
- b. *CK20* is considered a marker of neoplastic epithelial cells but previous studies have described *CK20* positivity in the blood of healthy subjects.
- c. In the current study, no *CK20* cell-equivalents were detected in the blood of healthy donors.
- d. False positive results can occur due to artifactual contamination or cross-contamination of samples.

**6. Based on the referenced article, select the ONE method that did NOT contribute to achieving optimal sensitivity and specificity for detection of *CK20*: [See J Mol Diagn 2006 8: 105-112]**

- a. Single round reverse transcriptase-polymerase chain reaction (RT-PCR).
- b. A primer overlapping adjacent exons to minimize co-amplification of unspliced DNA templates.
- c. Nested real-time RT-PCR.
- d. The first 5 mL of blood were discarded to avoid contamination with skin cells.

**The choices for the following questions, based on the review article about nucleic acid amplification testing for *Neisseria gonorrhoeae*, are numbered 1, 2, 3, and 4.**

**The answer key is:**

- a. only 1 and 3 are correct
- b. only 2 and 4 are correct
- c. only 4 is correct
- d. all are correct

**7. Based on the referenced review article about nucleic acid amplification testing (NAAT) for *Neisseria gonorrhoeae*, select the correct statement(s) about approaches to diagnosis and detection of *N. gonorrhoeae*: [See J Mol Diagn 2006 8: 3-16]**

- 1. Detection by Gram stain is very sensitive in men but relatively insensitive in women.
  - 2. Culturing *N. gonorrhoeae* is performed routinely on urine samples.
  - 3. NAAT approaches offer improved sensitivity compared to bacterial culture, particularly for asymptomatic patients.
  - 4. Hybridization assays are the most reliable of all approaches as they are not affected by polymerase chain reaction inhibitors.
- 
- a. only 1 and 3 are correct
  - b. only 2 and 4 are correct
  - c. only 4 is correct
  - d. all are correct

**8. Based on the referenced review article about nucleic acid amplification testing (NAAT) for *N. gonorrhoeae*, advantages of NAAT include: [See J Mol Diagn 2006 8: 3-16]**

1. Current commercial NAAT assays provide data on antibiotic resistance.
  2. Self-collected samples can be utilized.
  3. The specificity of NAAT is higher than that of bacterial culture for detection of *N. gonorrhoeae*.
  4. Sample handling is less difficult as nonviable organisms can be detected.
- a. only 1 and 3 are correct
  - b. only 2 and 4 are correct
  - c. only 4 is correct
  - d. all are correct

**9. Based on the referenced review article about nucleic acid amplification testing (NAAT) for *N. gonorrhoeae*, choose the correct statement(s) to complete the sentence: Inhibition of polymerase chain reaction: [See J Mol Diagn 2006 8: 3-16]**

1. can be caused by nitrites.
  2. can be detected by use of an internal control.
  3. can be caused by beta human chorionic gonadotropin.
  4. frequently occurs in urine samples.
- a. only 1 and 3 are correct
  - b. only 2 and 4 are correct
  - c. only 4 is correct
  - d. all are correct

**10. Based on the referenced review article about nucleic acid amplification testing (NAAT) for *N. gonorrhoeae*, mechanisms that may lead to false positive NAAT include: [See J Mol Diagn 2006 8: 3-16]**

1. Horizontal exchange of genetic sequences between *Neisseria* species.
  2. Loss of genetic signature from *N. gonorrhoeae*.
  3. Cross contamination of patient samples.
  4. Use of an internal control sequence in a duplex reaction.
- a. only 1 and 3 are correct
  - b. only 2 and 4 are correct
  - c. only 4 is correct
  - d. all are correct

**\*Disclosures:** Multiple authors of J Mol Diagn 2006 8: 51-61 disclosed a possible financial conflict of interest with Wyeth Pharmaceuticals. No authors of the other referenced articles disclosed any possible conflicts of interest.

**SEE EXAMINATION ANSWER SHEET - NEXT PAGE**

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**CME Questions # 1-10**

Answer	a	b	c	d
Question #1	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
Question #2	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
Question #3	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
Question #4	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
Question #5	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
Question #6	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
Question #7	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
Question #8	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
Question #9	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
Question #10	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
				<b>Name</b>
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1. You **must** be registered for the JMD CME Program prior to submission or you may register along with submission of your first Examination Answer Sheet.\*
2. Fill in the appropriate circle for each question to indicate your answer.
3. Enter your name and email address.
4. Mail or fax this completed Examination Answer Sheet to the AMP/ASIP JMD CME office.
5. Keep a copy of your Examination Answer Sheet for your records to compare with correct answers.
6. Your score and correct answers will be emailed to you within 14 days.\*\*

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