

# JMD CME Program in Molecular Diagnostics 2006

Association for Molecular Pathology *and the*  
American Society for Investigative Pathology

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## CME Questions # 41-50

(See February-September 2006 Examination Sheets for Questions #1-40)

**41. Microarray-based comparative genomic hybridization (array CGH) is a technique that evaluates DNA copy number alterations associated with chromosome abnormalities. Based on the referenced Review article and associated Commentary article, select the ONE statement that is NOT true: [See J Mol Diagn 2006 8: 528-533\* and J Mol Diagn 2006 8: 534-539]**

- Array CGH technology was first developed as a research tool for the investigation of genomic alterations in cancer and it is now being developed for clinical laboratory applications.
- Array CGH compares RNA content from two differentially labeled RNA populations – a test or patient cell population and a reference or control cell population.
- Arrays can utilize a variety of substrates such as oligonucleotides, cDNAs, or genomic fragments that are cloned in a variety of vectors such as plasmids, cosmids and artificial chromosomes.
- The resolution of an array is determined by the size of the nucleic acid targets and the density of coverage over the genome (the natural distance between these sequences located on the chromosome).
- The presence of benign copy-number variants (CNVs) and the incorrect assignment of genomic locations for some bacterial artificial chromosomes (BACs) are potential complications in analyzing array CGH results.

**42. Based on the referenced Review and Commentary articles that describe the potential applicability of array CGH in the diagnostic laboratory, select the ONE statement that is NOT true concerning the relative advantages of array CGH over fluorescence *in situ* hybridization (FISH): [See J Mol Diagn 2006 8: 528-533\* and J Mol Diagn 2006 8: 534-539]**

- Array CGH can detect DNA copy changes simultaneously at multiple loci in a genome.
- Array CGH can potentially detect deletions, duplications, or amplifications at any locus as long as that region is represented on the array, while FISH is limited by the number of probes that can be used simultaneously.
- The choice of a probe for FISH analysis is dictated by clinical suspicion or knowledge that a specific locus in the genome may have undergone copy-number change.
- FISH may be conducted on metaphase or interphase cells.
- FISH analysis on metaphase chromosomes is preferred for the identification of duplications.

**43. Gene expression profiles of human blood samples often use methods for globin mRNA reduction to increase the sensitivity of detection of transcripts of interest. Based on the referenced Technical Advance article concerning the effects of globin mRNA reduction methods on gene expression profiles, select the ONE statement that is NOT true: [See J Mol Diagn 2006 8: 551-558]**

- Current methods in use to reduce globin mRNA are based on peptide nucleic acid inhibitory oligonucleotides (“inhibitory oligo method”) and on biotinylated DNA capture oligonucleotides (“capture oligo method”).
- Both the inhibitory method and the capture oligo method were efficient at reducing globin mRNA and at increasing the sensitivity of transcript detection without loss of specificity.
- In assessing profiles from Jurkat cell line RNA and from blood RNA isolated using human PAXgene collection tubes, the authors found that the inhibitory oligo method had slightly better transcript detection sensitivity for cell line RNA, lowered signal variation for PAXgene RNA, and more similar profiles to controls than the capture oligo method.
- The capture oligo method required larger amounts of high quality RNA to yield sufficient cRNA amounts.
- Procedures for the capture oligo method are more complex and time consuming than those for the inhibitory oligo method.

**44. Familial hyperparathyroidism is characterized by calcium-insensitive hypersecretion of parathyroid hormone and increased cell proliferation. Based on the referenced article that describes mutation screening for two tumor suppressor genes linked to familial hyperparathyroidism, select the ONE statement that is NOT true: [See J Mol Diagn 2006 8: 559-566]**

- The hyperparathyroidism jaw-tumor syndrome gene *HRPT2* is a tumor suppressor gene located on chromosome 1 and consisting of 17 exons.
- Germline multiple endocrine neoplasia type I (*MEN1*) mutations and *HRPT2* mutations have been found in a majority of patients presenting with familial isolated hyperparathyroidism (FIHP).
- Denaturing high performance liquid chromatography (DHPLC) was used to scan for amplicons of *MEN1* and *HRPT2* that contained mutations and/or polymorphisms.
- Different melt domains in the exon 2 amplicon of *HRPT2* were used to determine the concurrent presence of common intronic polymorphisms and exonic mutations.
- There was decreased sensitivity of mutation detection by DHPLC for amplicons greater than 550 bp.

**45. Uveal melanoma is the most common primary cancer of the eye. Based on the referenced article that describes transcriptomic profiling of fine needle biopsy specimens of uveal melanoma, select the ONE statement that is NOT true: [See J Mol Diagn 2006 8: 567-573]**

- RNA analysis of primary uveal melanomas by transcriptomic profiling reveals two general class signatures associated with excellent versus poor prognosis.
- The class 2 signature predicted a high risk of metastatic death and was strongly associated with other predictors of poor prognosis such as epithelioid cytology, looping extracellular matrix patterns, and monosomy 3.
- Enucleation is performed on over 90% of uveal melanoma patients.
- RNA of sufficient quality and quantity was obtained from fine needle ocular aspirates of uveal melanomas to generate transcriptomic profiles with results that were significantly similar to those obtained from large tissue sections from the same tumor.
- A list of 45 probe sets was identified from the intersection of class discriminators in three different datasets to lay the groundwork for a clinical test.

**46. *Neisseria gonorrhoeae* is the causative agent of gonorrhea, but it is difficult to diagnose by culture. Based on the referenced article describing a molecular detection technique for *N. gonorrhoeae*, select the ONE statement that is NOT true: [See J Mol Diagn 2006 8: 574-581]**

- Of the many closely related species of the *Neisseria* genus, only *N. meningitides* and *N. gonorrhoeae* are primarily pathogenic to humans.
- Although culture is the gold standard for diagnosing *N. gonorrhoeae*, the bacteria does not survive very long outside the host, reducing the sensitivity of the culture technique.
- Nucleic acid amplification tests offer increased sensitivity compared to culture techniques however concerns have been raised about the specificity of such tests.
- The *porA* pseudogene of *N. gonorrhoeae* is a choice target for a nucleic acid amplification test of high specificity because it is absent in commensal *Neisseria* species and is sufficiently divergent from the *porA* gene of *N. meningitides* to be discriminatory between the two human pathogenic *Neisseria*.
- Like most pseudogenes, the *porA* pseudogene of *N. gonorrhoeae* is highly unstable.

**47. Prognosis in renal cell carcinoma has been based on clinical stage and nuclear grade. Some malignant tumors have shown relative up-regulation of type II hCG $\beta$  genes in relation to type I hCG $\beta$  genes. Based on the referenced article concerning the quantification of relative levels of mRNAs for the two types of hCG $\beta$  genes in renal tumor tissues, select the ONE statement that is NOT true: [See J Mol Diagn 2006 8: 598-603]**

- Expression of hCG $\beta$  mRNA in renal tumors was mainly caused by expression of type II genes.
- The prognostic value of hCG $\beta$  mRNA in renal carcinoma was evident from the association of expression with shorter disease-specific and overall survival.
- Expression of hCG $\beta$  mRNA was not detected in benign renal tissue.
- Forty percent of the tumor samples expressed hCG $\beta$  mRNA.
- In papillary and chromophobe renal tumors, the expression of hCG $\beta$  mRNA was strongly associated with shorter survival.

**48. Quantitative methods are often critical to the definition of tumor markers. Based on the referenced article, select the ONE statement regarding the technical assessment of hCG $\beta$  in relation to renal cancers that is NOT true: [See J Mol Diagn 2006 8: 598-603]**

- a. A non-quantitative RT-PCR assay was capable of detecting mRNA expression in renal tumors at a rate similar to that of the quantitative method.
- b. Serum levels of hCG $\beta$  have been demonstrated to serve as a prognostic marker in patients with renal cancer.
- c. The quantitative RT-PCR method used in this study revealed a surprising association of low levels of gene expression with adverse outcome.
- d. Immunohistochemical studies demonstrated hCG $\beta$  protein in some renal tumors but were unable to associate the results with prognosis.
- e. Alterations in hCG $\beta$  gene expression levels in renal cell carcinoma have been detected by expression profiling with microarrays.

**49. Molecular techniques have revolutionized the laboratory diagnosis of many viral infections. Based on the referenced article indicating the importance of early confirmation of dengue diagnosis and identification of serotype for epidemiologic purposes, select the ONE statement that is NOT true: [See J Mol Diagn 2006 8: 613-616]**

- a. Dengue fever and dengue hemorrhagic fever are caused by four antigenically similar viruses.
- b. Reverse transcriptase-polymerase chain reaction (RT-PCR) diagnosis is informative of serotype.
- c. Capture ELISA for dengue IgM antibodies is the method of choice for early detection of dengue virus in patients within five days of illness onset.
- d. Prompt response to vector control is important for interruption of dengue transmission.
- e. Infection by one serotype of the dengue virus does not provide cross immunity to infection by other serotypes.

**50. Diagnosis of dengue is difficult because symptoms are nonspecific and often mimic a wide range of other illnesses. A number of laboratory tests have been used to confirm clinical identification of the disease, although all have limitations. Based on the referenced article, select the ONE method that is currently NOT in general use: [See J Mol Diagn 2006 8: 613-616]**

- a. Dengue virus isolation and detection by indirect immunofluorescence.
- b. Semi-nested multiplex RT-PCR.
- c. Capture ELISA for IgM antibody.
- d. LigAmp assay for viral sequence genotyping.
- e. Detection of rise in IgG antibody in paired convalescent sera.

**\*Disclosures:**

**J Mol Diagn 2006 8: 528-533:** The authors are co-owners and board members of Signature Genomic Laboratories, LLC.

**SEE EXAMINATION ANSWER SHEET – NEXT PAGE**

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**CME Questions # 41-50**

<b>Examination Answer Sheet #5, Questions #41-50</b>					
Answer	a	b	c	d	e
Question #41	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
Question #42	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
Question #43	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
Question #44	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
Question #45	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
Question #46	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
Question #47	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
Question #48	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
Question #49	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
Question #50	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
<b>Name</b>					
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<b>CME ID# (For office use only)</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 of the year. \*
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 (along with your payment and CME Registration Form if you have not already registered\* ) 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.\*\*

\* Register online at [www.asip.org/register.html](http://www.asip.org/register.html) or you may submit your CME 2006 Registration Form with payment prior to, or along with, your first Examination Answer Sheet of the year. You may download the JMD CME Registration Form at [www.asip.org/CME/jmdCME.htm](http://www.asip.org/CME/jmdCME.htm) or [www.amp.org/CME/jmdCME.htm](http://www.amp.org/CME/jmdCME.htm).

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