A Review on molecular oncology testing in developing nations and research articles on extra alleles in fragile X testing and long noncoding RNAs as putative biomarkers for prostate cancer were selected for the November 2014 JMD CME Program in Molecular Diagnostics. The authors of the referenced articles, the planning committee members, and staff have no relevant financial relationships with commercial interests to disclose.


Questions #10-12 are based on: Wakeling EN, Nahhas FA, Feldman GL: Extra alleles in FMR1 triple-primed PCR: Artifact, aneuploidy, or somatic mosaicism? J Mol Diagn 2014, 16:689-696; http://dx.doi.org/10.1016/j.jmoldx.2014.06.006

Upon completion of this month’s journal-based CME activity, you will be able to:

- Understand the annual global incidence of cancer.
- Describe the infectious agents that may cause some cancer-related deaths in developing nations.
- Explain available tests that are devised specifically for resource-poor areas.
- Understand hepatitis B virus (HBV) and hepatitis C virus (HCV) infections.
- Describe tuberculosis and the select molecular tests that can detect it.
- Explain the Cancer Genome Atlas (TCGA) project.
- Describe portable test systems that can be used in the military.
- Understand prostate cancer (PCa) incidence and prostate-specific antigen (PSA) testing.
- Describe long noncoding RNAs (lncRNAs).
- Define Fragile X syndrome (FXS) and how it affects males and females.
- Explain the cause of FXS.
- Describe the characteristics of FXS premutation carriers.

1. Modern technology may address gaps in healthcare through rapid inexpensive automated test systems that identify and monitor the types of neoplasia prevalent in resource-poor areas. Based on the referenced Review, select the ONE statement that is NOT true: [See J Mol Diagn 2014, 16:601-611.]

   a. Noncommunicable diseases are projected to become the major global health burden in the near term, with cancer accounting for approximately one-quarter of this burden, of which, at least one-third is preventable.
   b. The annual global incidence of cancer is projected to increase from 5.2 to 15.4 million by 2030, with 7.5 million expected deaths.
   c. Over two-thirds of the burden will occur in low- and middle-income countries, wherein seven cancer types (lung, colon, breast, stomach, liver, cervical, esophageal) account for nearly two-thirds of incidents.
   d. In the world’s poorest countries compared to developed nations, women are more than twice as likely to die of their breast cancer, and children are up to 9-fold less likely to be cured of acute lymphoblastic leukemia.
2. In developing nations, nearly one-quarter of cancers are infection related. Based on the referenced Review, select the ONE statement that is NOT true: [See J Mol Diagn 2014, 16: 601-611.]

a. Four infectious agents account for over 80% of the burden: human papillomavirus (HPV), Helicobacter pylori, hepatitis B virus (HBV), and hepatitis C virus (HCV).

b. Epstein-Barr virus (EBV) adds a significant burden in several areas of the world.

c. Approximately 70% of infection-associated cancers occur in people under age 50.

d. Compared to more developed regions, less developed nations have more cancers of the stomach, uterine cervix, and liver, all three of which are infection-related.

3. Rapid low-cost devices are being developed to test for HPV DNA and RNA. Based on the referenced Review, select the ONE statement that is NOT true: [See J Mol Diagn 2014, 16: 601-611.]

a. A commercially designed test system has been devised specifically for resource-poor areas, and published data suggest that its performance is similar to a US Food and Drug Administration (FDA)--approved test.

b. The battery-powered bench top instrument requires neither electricity nor running water to perform hybrid capture of RNA probes bound to high-risk HPV DNA genomes.

c. The manufacturer states that the reagents are tolerant of temperature swings that may characterize a rural laboratory having spotty electricity for refrigeration.

d. The test can be performed by minimally trained technologists at 6-fold less cost and 3-fold less time than an FDA-approved assay, potentially permitting same-day intervention for HPV-positive patients.

4. HBV and HCV infections are common and predispose to hepatocellular carcinoma. Based on the referenced Review, select the ONE statement that is NOT true: [See J Mol Diagn 2014, 16: 601-611.]

a. Transfusion-mediated infection remains a concerning means of spread for HBV, HCV, and other pathogens in countries lacking a centralized system for blood collection and laboratory testing for transmissible agents.

b. Perinatal infection accounts for about half of the burden among the 500 million people with chronic HBV infection.

c. Vaccination is recommended for HBV-related cancer prevention, whereas treatment of HCV is associated with reduced cancer risk.

d. Viral genomes can be detected, characterized, and monitored using molecular tests, such as real-time quantitative PCR.

5. Tuberculosis is responsible for 1.7 million deaths per year. Based on the referenced Review, select the ONE statement that is NOT true: [See J Mol Diagn 2014, 16: 601-611.]

a. The risk of lung cancer increases 18-fold among tuberculosis patients.

b. Proposed mechanisms of mycobacteria-related carcinogenesis include long-term immune stimulation, neoangiogenesis, and DNA damage from reactive oxygen species.

c. Molecular tests can detect and speciate mycobacteria as well as predict drug resistance to assist clinicians in selecting rifampin, isoniazid, or second-line medications.

d. A PCR test system specifically designed to be rapid and user-friendly in low-volume testing laboratories has been developed to help guide appropriate therapy in tuberculosis-endemic regions.

6. The Cancer Genome Atlas (TCGA) project is a major step forward in cataloging mutation patterns and gene expression profiles in concert with traditional diagnostic histopathology. Based on the referenced Review, select the ONE statement that is NOT true: [See J Mol Diagn 2014, 16: 601-611.]

a. TCGA results to date confirm known cancer-related infections and provide new insights into the genetic underpinnings of neoplasia.

b. Multigene test panels can characterize signaling pathways driving tumor growth.

c. Genotyping is achievable on fresh, frozen, or fixed tissue in 30 minutes using an instrument platform that performs automated extraction followed by analysis to query 25 mutations in KRAS, BRAF, and PIK3CA genes.

d. A more practical test panel in hospitals lacking on-site pathology services might examine fine needle aspirate material from a mass lesion to help distinguish infection from tumor pending send out for a pathologist's definitive diagnosis days to weeks later.
7. Government-sponsored research has devised test systems for military and aerospace use, and some of these advances have been adapted for the benefit of civilian healthcare facilities. Based on the referenced Review, select the ONE statement that is NOT true: [See J Mol Diagn 2014, 16: 601-611.]

   a. In the 1990s, a briefcase-bound version of a thermocycler was developed that was later redesigned for clinical laboratory use.
   b. Currently, a system is being developed to test 15 nucleic acid targets in two hours with only 5 minutes of hands-on time.
   c. These devices tend to operate without electricity and have flexible test options with barcode readers to assure proper selection reagents for each protocol.
   d. Reagents are freeze dried, which makes them light weight to transport, and stable at room temperature for six months.

8. Despite advances associated with modern medicine, improvements in prostate cancer (PCa)-related mortality have been marginal at best. Based on the referenced article, select the ONE statement that is NOT true: [See J Mol Diagn 2014, 16:615-626.]

   a. According to the 2013 National Cancer Institute estimates, there will be 290,720 new PCa diagnoses this year; for 23,590 patients, it is likely to be fatal.
   b. Most men with PCa have indolent disease for which conservative therapy or an active surveillance approach would be more appropriate and would result in less treatment-related morbidity.
   c. A contributing problem has been the widespread use of prostate-specific antigen (PSA) testing.
   d. The PSA test has low specificity for cancer and cannot differentiate indolent and aggressive cancers.

9. Long noncoding RNAs (IncRNAs) are RNA transcripts >200 nucleotides in length. Based on the referenced article, select the ONE statement that is NOT true: [See J Mol Diagn 2014, 16:615-626.]

   a. IncRNAs exhibit cell type–specific expression and are localized to specific subcellular compartments.
   b. A number of IncRNAs are known to play important roles during cellular development and differentiation.
   c. Like microRNAs (miRNAs), IncRNAs are dysregulated in various medical conditions.
   d. IncRNA AK024556 (SPRY4-IT1) is up-regulated in human PCa, and siRNA-mediated knock-down of SPRY4-IT1 in PCa cells alters cellular growth and differentiation and increases the rate of apoptosis.

10. Fragile X syndrome (FXS) is the most common inherited form of intellectual disability. Based on the referenced article, select the ONE statement that is NOT true: [See J Mol Diagn 2014, 16:689-696.]

   a. FXS affects 1:3000 to 1:4000 females and 1:6000 to 1:8000 males.
   b. Males with FXS have moderate to severe intellectual disabilities, behavioral difficulties, macroorchidism, and characteristic facial dysmorphism.
   c. FXS females are usually more mildly affected than males.
   d. Females with FXS exhibit normal to mildly impaired intellect, learning difficulties, and emotional problems, including depression and anxiety disorders.

11. FXS is caused by loss of expression of the FMR1 gene located on chromosome Xq27.3. Based on the referenced article, select the ONE statement that is NOT true: [See J Mol Diagn 2014, 16:689-696.]

   a. FMR1 encodes the fragile X mental retardation protein (FMRP).
   b. FMRP is a RNA-binding protein that is highly expressed in neurons.
   c. The stability, subcellular localization, and translation of several mRNAs involved in synaptic structure and function are regulated by FMRP.
   d. Approximately 70% of FXS cases result from a CGG repeat expansion in the 5′ untranslated region (UTR) of FMR1.

12. Premutation alleles (55 to 200 CGG repeats in the FMR1 gene) are particularly unstable in female meiosis with repeats as small as 56 and 59 CGGs expanding to full mutations in one generation. Based on the referenced article, select the ONE statement that is NOT true: [See J Mol Diagn 2014, 16:689-696.]

   a. Approximately 1:151 to 1:178 females and 1:468 males in the U.S. are premutation carriers.
   b. In addition to the significant risk of having a child with a full mutation, premutation carriers are also at risk of developing other FMR1-related disorders.
   c. Up to 50% of female carriers will develop fragile X primary ovarian insufficiency, defined as cessation of menses by age 49.
   d. Fragile X–associated tremor ataxia syndrome is a late-onset progressive cerebellar ataxia with intention tremor that affects 30% of male and 8% to 16.5% of female premutation carriers over age 50.